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THE NATURAL HISTORY OF RHEUMATIC CARDIAC DISEASE: A STATISTICAL STUDY

I. ONSET AND DURATION OF DISEASE

ALFRED E. COHN, M.D.
AND
CLAIRE LINGG
NEW YORK

We are approaching the end of a study which has occupied us continuously for fifteen years. The task that was set was an attempt to describe the natural history of rheumatic fever, presumably a single disease. The results have been accomplished through the cooperation of many persons of good will.[1] The brief descriptions and the generalizations now possible could not have been made without the great labor or the continued reflection which have been devoted to this task.

It is not too much to say that we know the behavior of rheumatic fever, at least in this locality and at this time. It is possible now to separate knowledge which is complete and definitive from information which is partial and tentative. It is possible, furthermore, to interpret the latter in terms of the former. The length of time during which we have been familiar with this subject has made it possible to reduce the descriptions to relatively few categories. It has been as important to us to be explicit where knowledge is full as we have known it to be desirable to be circumspect where it is partial.

These introductory remarks would be incomplete unless emphasis was placed on the environment in which this study took place. Only an organization such as the New York Heart Association, a committee of the New York Tuberculosis and Health Association, formed of men and women of professional stature equal to theirs, could have supplied the thought and guidance which served first as the basis and later as a background for these labors.

When this study was undertaken, directly at the end of the first great war, alarm was beginning to spread at what seemed to be a rapid increase in deaths from cardiac diseases. At first it was impossible to find explanations for this appearance. It was necessary to explore avenues and to ask questions designed to clarify the situation. On the result depended the means to be employed in the care of the public health. The kind and nature of the diseases, the degree of their communicability, the kind and age of the persons affected, the duration of the phases of each kind of disease, the duration of the diseases, the numbers of persons subject to each variety of ailment, what institutional arrangements were necessary at the various stages and what equipment was desirable for diagnosis and treatment—all these needed to be canvassed.

The first contribution that illuminated any of these vexed questions was made by Wyckoff and Lingg,[1a] who described the distribution of cases in an adult cardiac clinic at the Bellevue Hospital in New York City. Theirs was a thorough study of the incidence and classification of the cardiac diseases as a whole. They found that to the total rheumatic fever contributed one fourth, arteriosclerosis two fifths, syphilis one tenth, cases of unknown origin one tenth and cases of all other origins one tenth. They found also that 90 to 95 per cent of rheumatic cardiac diseases occurred before 50 years and more than half of them before 30; that half the cases of syphilis developed before 50, and that 80 to 95 per cent of cases of arteriosclerosis developed after 50 years of age. It was not difficult after their investigation to decide that cases of rheumatic origin deserved attention first. If there were no other reason for this selection, the fact of its occurring in young people and of being conceivably preventable would have been justification enough.

How the matter lay, then, is clear from this quotation:[2]

"No doubt we shall learn much from the changes in shape of specific death rate curves. We must study whether, if these changes have occurred, they have

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This general paper was presented in outline before the Graduate Fortnight of the New York Academy of Medicine, Oct. 23, 1941.

From the Hospital of the Rockefeller Institute for Medical Research and the Heart Committee of the New York Tuberculosis and Health Association, Inc.

Part II, on the manifestations of rheumatic activity: recurrence, severity of infection and prognosis, will appear in the next issue of THE JOURNAL.

The statistical assistants on whom we rely for the collection and refinement of the original material as well as for the subsequent statistical analysis and arrangement comprise Rose Goldman, Rita Goldsmith, Lily Popper, Eve Saper, Harriet Steinhilber and Alice Whittemore. Without the devoted cooperation such as they gave us these studies could not have been made.

1. The Commonwealth Fund and the Metropolitan Life Insurance Company gave financial assistance in the early years of this investigation; the members of the Committees on Research, on Clinics and on Criteria of the New York Heart Association gave technical advice and assistance; many physicians and social service workers in the cardiac clinics recorded in detail, week after week, histories and physical examinations; reports and abstracts of medical records were sent to us by hospital superintendents and record librarians, convalescent homes, social agencies and many physicians in private practice; the directors of pathologic laboratories and the medical examiner's office of the health department of New York City made available copies of autopsy protocols, and Dr. Clarence E. de la Chapelle reviewed postmortem reports; the board of health of New York City made available to us death certificates; the WPA provided clerical and statistical assistance and traced the whereabouts of thousands of patients no longer attending the clinics and obtained from them after-histories, which made it possible for us to complete the records up to the year 1938-1939 of 97 per cent of the patients, both dead and living; Miss Anne Spreemann of the staff of the New York Heart Association ably supervised this work. The Board of Education, the Department of Public Welfare, numerous other social agencies, the New York City branch of the U. S. Post Office and the Consolidated Edison Company all aided in locating patients. The patients themselves and their friends supplied us with information essential to completing the life histories in the large number of cases.

1a. Wyckoff, J., and Lingg, Claire: Statistical Studies Bearing on Problems in Classification of Heart Diseases: II. Etiology in Organic Hearth Disease, Am. Heart J. **1**: 446, 1926.

2. Cohn, A. E.: Statistical Studies Bearing on Problems in the Classification of Heart Diseases: I. Introduction, Am. Heart J. **1**: 442, 1926.

occurred as the result of efforts at prevention of infectious heart disease in early life or for causes related to the saving of life at other decades and from other diseases. We must learn what percentage (whether the number of cases remains stationary or increases or decreases) is prevented, what percentage cured, what percentage senescent. Only by analyses such as these shall we learn the nature of the problem with which we must deal, and on what aspect of it is the major emphasis most intelligently to be placed.

"There are many other problems for which our methods may yield solutions: studies in the natural history of these diseases; their duration, and whether this is modified, and how much, by differences in social and economic environment; does symptomatology vary with class and with age; what is the bearing of age on the possibility of recovery; what influences are exerted on their course by treatment; of what use are certain forms of treatment, such as rest, work, homes for convalescent patients, operations on portals of entry, such as teeth and tonsils."

Familiarity with the study of acute infectious illnesses has accustomed physicians to viewing processes of disease as taking place within short periods of time. The exanthemas, lobar pneumonia, typhoid, all fall into this group. The beginning, the middle and the end, together with the sequelae, fall easily within the purview of single observers. Even pulmonary tuberculosis does not fall outside this category. The situation is quite different in such other diseases as those which are the concern of these studies. They are all long drawn out and endure in rheumatic fever about thirteen years on the average, in syphilis perhaps half as long again and in the later arteriosclerotic forms, whether long or short, the onset often being difficult to define. In any case the whole of the life of persons afflicted by this group of ailments has not often been the subject of surveys by single physicians. Because of this fact episodes occurring in the course of such illnesses have attracted attention and study, rather than the processes themselves in long drawn out continuity. These have almost necessarily escaped description from the point of view of the whole of their natural history because a sufficient number of cases exhibiting such phenomena have not been investigated by properly trained and interested physicians.

Discussion of the natural history of rheumatic fever has accordingly been made difficult by the partial descriptions that have been available. The facts can be and indeed have been analyzed and presented from several more or less incompatible points of view. The view of private practitioners is necessarily limited by their personal experience. That of attending physicians of hospitals is circumscribed by the procedure of admission and discharge, often with incomplete knowledge of the subsequent history of patients. Public health officers describe the course of events naturally in terms of vital statistics.

The point of view in this study corresponds to none of these. It began and has continued to regard solely the natural history of this disease as exhibited by the continued histories of given individuals, from its onset until its end in these same individuals. This study is based accordingly not on cross sections, not on impressions, not on statistical averages but on histories literally representing courses of events. Because this was the plan, it has been possible to study aspects of the disease in their context. It is known, for example, that a certain phenomenon, if it appeared in a child, could subsequently be observed as it evolved in the later history of that individual and so could be related causally to its presence at earlier stages. The development of rheumatic phenomena is known therefore in continuity. Truth can be discovered no doubt also by other technics, as for example by random sampling of phenomena but, if it is a virtue, this investigation can claim knowledge derived from close observation together with the management and treatment of the very individuals whose illnesses have been analyzed. From this point of view the cases studied have the kind of value to be found in descriptions of cases reported by private practitioners.

The methods that have been employed are in essence not new, but they have been scrutinized afresh in order to fit the current uses to which they were put. To collect information of so large a number of cases it was necessary to define carefully the terms that were used. The selection of the terms was itself a matter of prime consideration. The Committee on Criteria of the New York Heart Association made these selections. It decided on and published appropriate definitions.[3] This procedure eliminated vagueness and confusion. Since the number of cases to be studied was large, it was necessary to record the histories in ways that made enumeration readily possible. Charts were therefore designed in which answers were entered in accordance with properly formulated questions. The questions were so put that the answers were as nearly as possible unequivocal. The charts consisted of parts so as to provide the opportunity to enter for each patient his history, his physical examination and his subsequent course. These charts were made in duplicate, the originals being retained by the clinic in which a patient was treated, the carbon copy being brought for file and subsequent analysis to the central office.[4]

Besides criteria and methods of recording, the ends in view could not have been accomplished had not the Committee on Cardiac Clinics seen to it that suitable quarters and adequate equipment were available.[5] In the early years physicians who attended the cardiac clinics met frequently for consultation on all the methods used. These conferences made reasonable uniformity of view and usage possible. Physicians willing to accept these methods constituted the indispensable cornerstone of the enterprise. But none of this apparatus could have sufficed had it not been for the statistical assistants provided by the New York Heart Association. It was their duty to attend clinics, to see to the upkeep of the records and more especially to the uniformity in the use of nomenclature and symbols which had been decided on, and finally to assist in completing, editing and analyzing the data.

If there is doubt of the value of results such as these, the doubt must, it seems, rest on popular conceptions of the nature of statistics. What physicians require and what after all they must have in the practice of medicine is information twofold in nature. They must know about the general movements of diseases, or their natural history; but they desire also a knowledge of methods which make applicable to individual cases the general considerations to which reference has been made. The difficulty is here. Except as far as the former aids an

3. Nomenclature and Criteria for Diagnosis of Diseases of the Heart, New York Heart Association (Heart Committee of the New York Tuberculosis and Health Association), New York, 1939.

4. Clinical Charts Recommended by the Heart Committee of the New York Tuberculosis and Health Association: The Plans for Their Use, Am. Heart J. **2**: 655, 1927.

5. Standard Requirements for a Cardiac Clinic, New York Heart Association, New York, 1936.

understanding of the latter, it can scarcely be pretended that the statistical or general method can be a useful practical instrument. Why this is so demands perhaps some discussion:

"The search for law in biology and of course in medicine rests on the conception that the discovery of laws has served the physical sciences in extraordinarily useful ways. There can be no doubt of the soundness of this belief. But precisely what the analogy is between law and the individual in the physical world, and law and the individual in the biological one, requires precise definition—more precise indeed than is usually accorded to this matter. If there is a difficulty it lies, we believe, in misunderstanding this relation of law to the individual in the physical world. The view we take may be illustrated. In the case of the gas laws for instance, beginning with Boyle, a number of statements have been made which permit accurate predictions of the behavior of volumes of gas; that these laws do not describe the behavior of individuals within the volume is amply demonstrated by reflecting on the fact that the kinetic theory assumes violently diverse and unpredictable behavior on the part of the individual molecules in these volumes. The laws apply to the mass, the volume, the average; they make no statements concerning individual performance. And yet the laws are invaluable; they and their kind are the basis of calculation in the practical as well as in the theoretical world. In biology and in medicine, just as in physics, it is not to the individual that the laws, whatever they are or may be discovered to be, apply. Individuals represent deviations from any law both in biology and in physics. Deviation is the fate of the individual; uniformity in the sense of identity either of being or of behavior scarcely exists. The general behavior of patients afflicted by typhoid fever or the general behavior of mobs may be known, but to know these phenomena has relatively speaking little meaning in understanding or in predicting the conduct of any individual in a mob or in making an accurate prognosis, based on general experience in the case of any patient suffering from typhoid fever. And yet no one denies that general statements can be made and are useful in physics and in psychology, or that general statements on prognosis and on the natural history of diseases have value. General statements and inference in individual instances each have their domain of eminent usefulness. Harm results only when the nature and objects of the two are confused. Whether in the natural history of any one of the cardiac diseases, or in an estimation of prognostic values, or in the measure of success of a therapeutic agent, or of the degree of relevance of social or economic advice, the aim of such studies as this is the attempt to understand general movement. No other indeed is possible. Because it is the plain teaching of the history of science, the Research Committee of the New York Heart Association believes that the ability to attain orientation of this sort is indispensable in envisaging the probable course of any individual life or of any individual act. Thought and action would otherwise be chaos." [6]

LITERATURE

The problem of what reference should be made to the literature of this subject has been a source of some concern. It has a large extent and very great value. Particular aspects must necessarily receive mention and comment in the text. But since these researches concerned an analysis of a large body of fact assembled in a somewhat novel fashion, it seemed more important to let the facts speak for themselves than to match them with data already available. Where there is conflict in interpretation this will of course take place.

Probably the earliest statistical report on this disease is to be found in Haygarth's [7] monograph on acute rheumatism published in England in 1805. "Among the higher and middle ranks of society," says the author, "I have noted and classed the cases of 10,549 patients from 1767 to 1801; also clinical reports of a large number of diseases among persons in the lower ranks of life, being cases of all in- and out-patients at the Chester Infirmary for thirty-one years." After eliminating cases of nodosity of the joints, tic douloureux, sciatica, lumbago and other conditions there still remained 470 cases of rheumatism. Since only 170 were febrile, these alone were included in his analysis of "acute rheumatism." In numerous tables he described the disease with regard to sex, age, seasonal incidence, latent periods, joints involved, pulse rate, urine and blood tests. This is probably the first accurate account of the natural history of polyarthritis.

Eighty-four years later, in 1889, Cheadle [8] published his lectures delivered before the Harveian Society of London on "The Various Manifestations of the Rheumatic State as Exemplified in Childhood and Early Life," in which he analyzed tables published in 1888 by the Collective Investigation Committee of the British Medical Association. These tables were based on reports of observations on 655 cases of acute rheumatism furnished by medical practitioners of the United Kingdom from 1882 to 1886. Among the factors considered were age, sex, occupation, locality and atmosphere, previous illnesses, influence of treatment, duration of fever, pain, extent of joint disease, complications, relapses, cutaneous eruptions, subcutaneous nodules, sequelae and deaths.

When after World War I it was pointed out that the death rate from cardiac diseases seemed to be rising, certain facts began to be subjected to more searching analysis in order to learn what actually was the situation in respect to these diseases. In 1927 a study of mortality curves for a period of fifty years made clear that the fall in rate in infectious diseases was intimately related with the rise in the cardiac ones.[9] But five years later,[10] in 1933, closer scrutiny of the data led to the inference that the increase in the cardiac death rate was relatively slight and that changing fashions in diagnoses were responsible for the apparently great increase.

In the years following the war many studies of rheumatic fever and rheumatic cardiac disease began to be reported. Among the more important statistical studies are those of the London County Council,[11] the Medical Research Council [12] and the Ministry of Health [13] in

6. Quoted by Pearl, Raymond: Introduction to Medical Biometry and Statistics, ed. 2, Philadelphia, W. B. Saunders Company, 1930, p. 24.

7. Haygarth, John: A Clinical History of Diseases: I. A Clinical History of the Acute Rheumatism, London, 1805.

8. Cheadle, W. B.: The Various Manifestations of the Rheumatic State as Exemplified in Childhood and Early Life, lectures delivered before the Harveian Society of London, London, Smith Eldor & Co., 1889.

9. Cohn, A. E.: Heart Disease from the Point of View of the Public Health, Am. Heart J. **2**: 275, 1927.

10. Cohn, A. E., and Lingg, Claire: Heart Disease from the Point of View of the Public Health—1933, Am. Heart J. **9**: 283, 1934.

11. London County Council: Annual Report of the Council, 1923, Public Health, London, 1924, iii; 1937, 3, part 2, 44.

12. Medical Research Council; Child Life Investigations; Social Conditions and Acute Rheumatism, London, 1927.

13. The Incidence of Rheumatic Disease, Reports on Public Health and Medical Subjects, No. 23, Ministry of Health, London, 1924. Acute Rheumatism in Children in Its Relation to Heart Disease, ibid. No. 44, 1927.

England, and the recent investigations of Hedley [14] of the United States Public Health Service. During the past two decades studies based on the clinical observation of series of patients, ranging in number from somewhat less than 100 to about 1,000, include in England and Wales the work of Poynton,[15] Coombs,[16] McSweeney,[17] Findlay,[18] Coates,[19] Campbell and Warner,[20] Miller,[21] Horder,[22] Brenner,[23] Dally,[24] Grant,[25] Hill [26] and Schlesinger,[27] and in this country the work of Mackie,[28] White,[29] Wilson,[30] Shapiro,[31] Sutton,[32] Jones,[33] Kaiser,[34] Paul,[35] Davis and Weiss,[36] Willius,[37] Ash,[38] Clawson,[39] McLean,[40] Leonard,[41] Juster,[42] Stroud,[43] Coburn,[44] Swift,[45] Taran,[46] Boas,[47] Thayer,[48] McCulloch and Irvine-Jones [49] and preliminary studies [50] made in collaboration with the Committee on Research of the New York Heart Association.

These studies deal with various aspects of the disease, notably its prevalence, familial and seasonal incidence, age at onset, its various manifestations and cardiac implications. Unfortunately this vast amount of data cannot be successfully pooled because of a lack of uniformity in observations and definitions, because the groups of cases analyzed are themselves limited either as to age, some having been selected from pediatric services only, and others from clinics and wards specified for adults; or as to source, comprising in some instances hospital admissions, in others ambulatory patients in public or private practice and in still others cases selected from postmortem records. Unfortunately too the criteria of statistical analysis that were employed have usually not been defined. The failure to take into consideration recognized, simple statistical procedure has often resulted in contradictory and controversial conclusions.

MATERIAL FOR STUDY

This study of rheumatic cardiac disease has been conducted on the basis of records of some 12,000 patients prepared by the New York Cardiac Clinics. Of these 3,129 are dead.[51] There were male and female patients

14. Hedley, O. F.: Mortality from Rheumatic Heart Disease in Philadelphia During 1936, Pub. Health Rep. **52:** 1907, 1937; Incidence of Rheumatic Heart Disease Among College Students in the United States, ibid. **53:** 1635, 1938; Trends, Geographical and Racial Distribution of Mortality from Heart Disease Among Persons 5-24 Years of Age in the United States During Recent Years (1922-1936): A Preliminary Report, ibid. **54:** 2271, 1939; Rheumatic Heart Disease in Philadelphia Hospitals, ibid. **55:** 1599, 1940.

15. Poynton, F. J.; Paterson, Donald, and Spence, J. C.: Acute Rheumatism in Children Under 12 Years of Age, Lancet **2:** 1086, 1920.

16. Coombs, C. F.: Rheumatic Heart Disease, New York, William Wood & Company, 1924; The Incidence of Fatal Rheumatic Heart Disease in Bristol, 1878-1913, Lancet **2:** 226, 1920; Thirty Years Progress in the Study of Rheumatic Heart Disease, Bristol Med.-Chir. J. **50:** 93, 1933.

17. McSweeney, C. J.: Acute Rheumatism in Childhood, Lancet **1:** 959, 1928; Studies in Juvenile Rheumatism, Arch. Dis. Childhood **6:** 367 (Dec.) 1931.

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19. Coates, Vincent, and Thomas, R. E.: Rheumatic Infection in Childhood, Lancet **2:** 326, 1925.

20. Campbell, Maurice, and Warner, E. C.: A Study of Rheumatic Disease in Children, Lancet **1:** 61, 1930.

21. Miller, Reginald: Discussion on the Etiology and Treatment of Heart Disease in Early Life, with Special Reference to the Prevention of Chronic Cardiac Insufficiency, Brit. M. J. **2:** 702, 1923; Report on the Environmental and Other Predisposing Causes of Rheumatic Infection, (supp.) Brit. M. J. **2:** 5 (July 3) 1926.

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25. Grant, R. T.: After-Histories for Ten Years of a Thousand Men Suffering from Heart Disease: A Study in Prognosis, Heart **16:** 275, 1933.

26. Hill, N. G.: The Etiology of Juvenile Rheumatism, Brit. J. Child. Dis. **27:** 161, 1930.

27. Schlesinger, Bernard: Public Health Aspect of Heart Disease in Childhood, Milroy Lectures, Lancet **1:** 594, 1938.

28. Mackie, T. T.: Prognosis and Treatment of the Rheumatic Infection, Am. Heart J. **3:** 31, 1927.

29. White, P. D.: The Incidence of Endocarditis in Earliest Childhood, Am. J. Dis. Child. **32:** 536 (Oct.) 1926.

30. Wilson, May G.: Rheumatic Fever, Commonwealth Fund, New York, 1940. Ingerman, Euginia, and Wilson, May G.: Rheumatism: Its Manifestations in Childhood Today, J. A. M. A. **82:** 759 (March 8) 1924.

31. Shapiro, M. J.: The Natural History of Childhood Rheumatism in Minnesota, J. Lab. & Clin. Med. **21:** 564, 1936.

32. Sutton, L. P.: Observations on Certain Etiologic Factors in Rheumatism, Am. Heart J. **4:** 145, 1928. Sutton, L. P., and Dodge, K. G.; Relationship of Sydenham's Chorea to Other Rheumatic Manifestations, Am. J. M. Sc. **195:** 656, 1938.

33. Jones, T. D., and Bland, E. F.: Clinical Significance of Chorea as a Manifestation of Rheumatic Fever, J. A. M. A. **105:** 571 (Aug. 24) 1935.

34. Kaiser, A. D.: Factors That Influence Rheumatic Disease in Children—Based on a Study of 1,200 Rheumatic Children, J. A. M. A. **103:** 886 (Sept. 22) 1934.

35. Paul, J. R.: Age Susceptibility to Familial Infection in Rheumatic Fever, J. Clin. Investigation **10:** 53, 1931; The Epidemiology of Rheumatic Fever: A Preliminary Report, for the American Heart Association, New York, Metropolitan Life Insurance Company, 1930. Paul, J. R., and Leddy P. A.: The Social Incidence of Rheumatic Heart Disease: A Statistical Study in Yale University Students, Am. J. M. Sc. **184:** 597, 1932.

36. Davis, David, and Weiss, Soma: The Relation of Subacute and Acute Bacterial Endocarditis to Rheumatic Endocarditis: A Study of 66 Cases with Necropsies, New England J. Med. **208:** 619, 1933; Rheumatic Heart Disease: I. Incidence and Role in Causation of Death: A Study of 5,215 Consecutive Necropsies, Am. Heart J. **7:** 146, 1931; II. Incidence and Distribution of the Age of Death, ibid. **8:** 182, 1932; IV. The Life History of the Severe Form of the Disease, ibid. **10:** 486, 1935.

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(Footnotes 40, 41 and 42 in next column)

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43. Stroud, W. D.; Goldsmith, M. A.; Polk, D. S., and Thorpe, F. Q.: Ten Years' Observation of Children with Rheumatic Heart Disease, J. A. M. A. **101:** 502 (Aug. 12) 1933.

44. Coburn, A. F.: The Factor of Infection in the Rheumatic State, Baltimore, Williams & Wilkins Company, 1931.

45. Swift, H. F.: Rheumatic Fever, in Cecil's Textbook of Medicine, ed. 4, Philadelphia, W. B. Saunders Company, 1936; Rheumatic Fever, Am. J. M. Sc. **170:** 631, 1925.

46. Taran, L. M.: Rheumatic Cardiac Disease in Childhood: A Statistical Study, Am. J. Dis. Child. **50:** 840 (Oct.) 1935.

47. Boas, E. P.: Rheumatic Fever in Adult Puerto Rican Immigrants, Am. J. M. Sc. **182:** 25, 1931.

48. Thayer, W. S.: Analysis of Eight Hundred and Eight Cases of Chorea, with Special Reference to Cardiovascular Manifestations, J. A. M. A. **47:** 1352 (Oct. 27) 1906.

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51. The patients were treated in clinics over a period of years ranging from 1923 to 1938. Of the records analyzed, 30 per cent were derived from clinics in city hospitals and 70 per cent from clinics in voluntary hospitals. About 70 per cent were contributed by clinics in the borough of Manhattan, thirteen for adults and twelve for children. The hospitals represented were Bellevue, Beth Israel, Fifth Avenue, Joint Diseases, New York Nursery and Childs, New York, New York Infirmary for Women and Children, New York Post-Graduate, New York Polyclinic, St. Mark's, Babies, Lenox Hill, as well as the Cornell Medical School and New York University Medical College cardiac clinics and clinics attached to the Bowling Green Neighborhood House and Greenwich House Settlement. In addition, 15 per cent were contributed by two clinics for adults and three for children in the borough of Brooklyn: Brooklyn, Jewish, Cumberland and Kings County hospitals; 8 per cent by two clinics for adults and one for children in Morrisania City and Montefiore hospitals in the Bronx; 5 per cent by a clinic for adults and one for children in St. John's Hospital, Queens; the clinic for after-care conducted by Irvington House contributed records from clinics in all the boroughs of New York City. Of these, 6 per cent were derived from clinics not cooperating with the New York Heart Association. Clinics in Philadelphia—in the Graduate, Woman's, Philadelphia General, Presbyterian, Lankenau, Misericordia, St. Christopher's and Abbington Memorial hospitals—contributed 4 per cent of the records. Altogether, only 8 per cent of the patients were treated in more than one clinic.

ranging in age from early childhood throughout the span of their surviving lives. It is in the interest of simplicity to describe the course of events in rheumatic fever first as exhibited by those who have died. Completed lives such as these render unequivocally reliable the inferences which are drawn concerning them—their course and prognosis. To these results may be added those modifications which apply to the living.

When they first came under observation in the clinics, 22 per cent of the patients were less than 10 years old, 45 per cent were under 15, and 53 per cent under 20; 13 per cent were in their twenties, 16 per cent in their thirties, 12 per cent in their forties and 6 per cent 50 years or older. About half, in short, were under 20 and half over 20.

Race.—The hospitals in New York City from which 94 per cent of the records came are situated in districts in which there is no large Negro population. Only 5 per cent therefore of the records analyzed were of Negroes. This study concerns itself consequently primarily with the occurrence of rheumatic fever in the white races.

Sex.—The supposition is general that girls are more often afflicted than boys, but when so large an experience as this is available it appears that this is not the

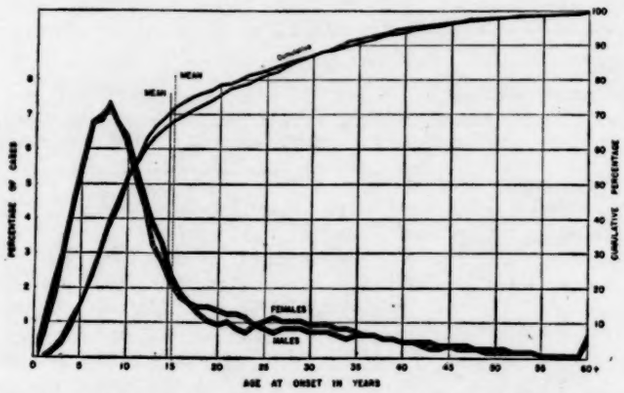

Chart 1.—Rheumatic cardiac disease. Onset usually in childhood, especially between the ages of 5 and 10 years, with maximum rate at age 8.

case—the two sexes are afflicted in equal numbers. There were 1,566 males and 1,563 females.

Age at Onset.—The ages found in this study at which rheumatic fever begins deserves credence because on close scrutiny the records exhibit a high degree of probable correctness. In the absence of a specific diagnostic test it is often difficult to be certain of the presence of rheumatic infection. By onset is meant, therefore, the first clinical manifestation of the disease. Since many patients first came under observation in the clinics some time after the onset (one fourth within less than a year and one half within three years thereafter), in order to date it correctly, every effort was made to obtain a reliable history. Past medical records were investigated in order to try to confirm the patient's recollection and so to lessen the chances of regarding a recurrence as the initial disorder.

In most of the published reports dealing with the age at onset, the cases analyzed are grouped according to age. If the analysis is based on children's clinics, the onset cannot escape being regarded as early; if based on adult clinics, late. In this study there is no loading in favor of any age.

It is clear (chart 1) that there is a slight difference between the sexes in the age at onset. The mean age for males is 14.5 ± 0.3 years and for females 15.0 ± 0.3 years. The difference 0.5 ± 0.136 may be considered statistically significant. The age at onset is on the average slightly higher in females than in males.

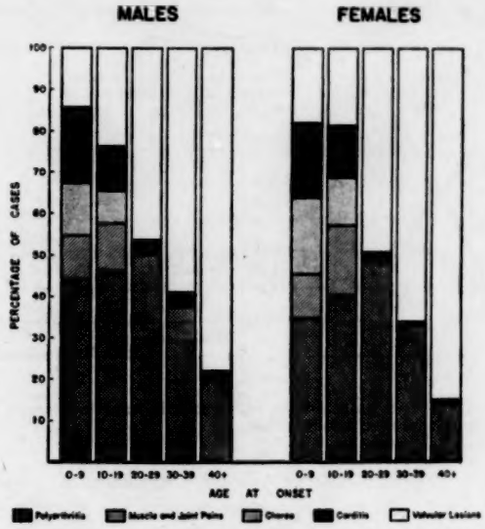

Chart 2.—In the young onset of rheumatic cardiac disease is characterized by polyarthritis in about one half and by carditis and chorea in about one third each. In adult life onset is characterized chiefly by polyarthritis and, with advancing age, by appearance of valvular lesions alone.

Rheumatic fever may begin at any age, but it begins more often at about 8 years than at any other age. At 15, the mean age at onset, 70 per cent of persons afflicted have already acquired the disease.

Year of Onset.—The calendar years in which these patients acquired the disease ranged from 1870 to 1938. In 7 per cent the onset occurred before 1900, in 11 per cent between 1900 and 1909, in 24 per cent between 1910 and 1919, in 45 per cent between 1920 and 1929 and in 13 per cent after 1930.

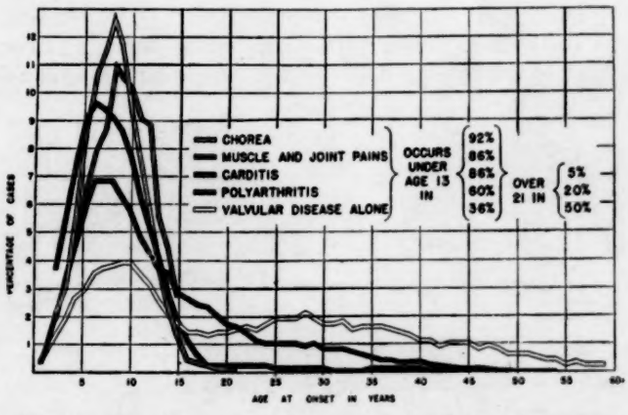

Chart 3.—Rheumatic cardiac disease. Age distribution of first manifestations.

INITIAL MANIFESTATIONS

In studying the manifestations of rheumatic fever, whether in the young or in the old, the similarity between males and females is close enough so that a description of one will do for the other (chart 2). If the usual manifestations of rheumatic fever are taken to be inflammation of the joints, muscle and joint pain, chorea and carditis, and if these taken together are regarded as infectious manifestations, it is evident that

among those in whom the disease is acquired before the age of 10 infection is the characteristic form of onset in over 85 per cent of cases. After 40 a little more than 20 per cent exhibit this form of the disease. Before 20 muscle and joint pains and chorea account for 20 per cent of cases, but after 20 these forms tend to disappear.

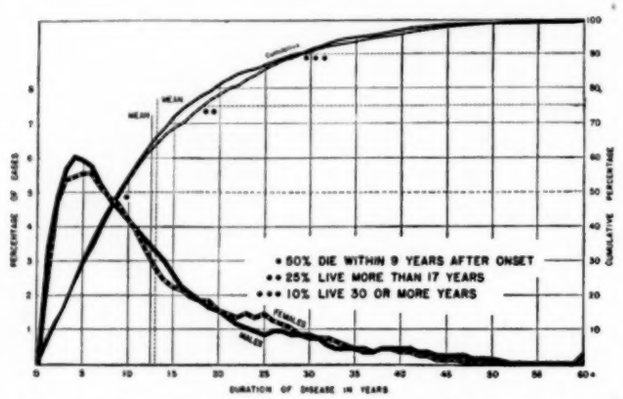

Chart 4.—The mean duration of rheumatic cardiac disease is about thirteen years from onset to death.

Instead, polyarthritis or valvular lesions alone are found. The picture becomes totally reversed. Before 10, valvular lesions alone are the first manifestation in only about 15 per cent of cases, after 40 in almost 80 per cent.

It need scarcely be pointed out that, though this is the distribution of first manifestations, numerically the group after age 40 is small and amounts to not more than 5 per cent of the total.

As initial phenomena for dating the onset of rheumatic fever the meaning of muscle and joint pains has often been called in question. How to be certain when they are significant is difficult and requires definition. In this study they are so regarded (in 281 cases or 9 per cent, table 1) only when additional evidence appeared later. It did so within one year in one third and within three years in almost half of the cases.

That acute inflammation of the joints is almost twice as common as active carditis in young persons is contrary to the general impression. An explanation for this

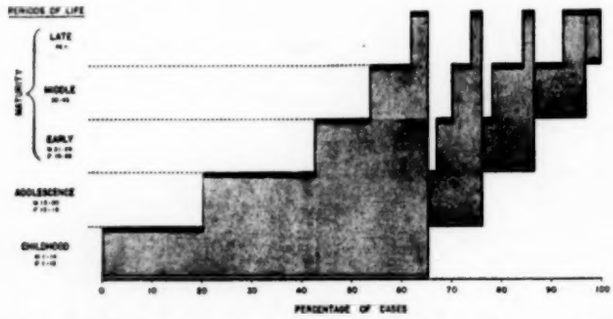

Chart 5.—Rheumatic cardiac disease. Two thirds of all cases begin in childhood, one tenth in adolescence; 20 per cent are fatal in childhood, another 25 per cent in adolescence; less than 25 per cent begin in adult life; about 15 per cent of the patients survive age 45. Periods of life: late maturity, 46 +; middle maturity, 30-45; early maturity, males 21-29 and females 19-29; adolescence, males 15-20 and females 13-18; childhood, males 1-14 and females 1-12. The light barred line indicates the age period in which disease began and the heavy line that in which death occurred; the vertical distance between the two indicates the duration of life.

is the fact that many cases were recorded first not during but shortly after the first attack of rheumatic fever. In the matter of recollection and emphasis it is not an uncommon experience to discover that what impresses physicians are valvular lesions. But in the mothers and in patients it is the multiple disorders of the joints. No doubt carditis is often present as well.

Although it is clear that rheumatic fever is a disease occurring predominantly in childhood and early adolescence, and although the relative frequency of its manifestations is as has been described, the age distribution of these manifestations as first phenomena permit a somewhat more detailed analysis (chart 3). It has already been said that chorea comes practically to an end at the age of 20. In point of fact there are few cases after 15. The greatest number actually occur at about 8 years of age. Indeed, no other manifestation is so centered on a single age. Carditis takes its maximum toll at about 6 years, polyarthritis from 6 to 8 years and muscle and joint pains from 8 to 10 years. When valvular disease occurs alone it is most commonly recognized at 9 and 10 years. As incipient manifestations only polyarthritis and valvular lesions are to be found in any considerable number after 15 (chart 3, table 2). Rheumatic fever appears, then, in various forms and each form has statistically an age distribution of its own.

TABLE 1.—*Type of Onset*

Type of Onset	Both Sexes		Males		Females	
	Number	Per Cent	Number	Per Cent	Number	Per Cent
Carditis	389	12.4	198	12.6	191	12.2
Murmur	886	28.3	426	27.2	460	29.4
Polyarthritis	1,262	40.3	682	43.5	580	37.1
Muscle and joint pains	281	9.0	128	8.2	153	9.8
Chorea	311	9.9	132	8.4	179	11.4
Total	3,129	99.9	1,566	99.9	1,563	99.9

TABLE 2.—*Onset of Disease, by Age, Sex and Manifestation*

First Manifestation	Sex	Number of Cases	Age					
			Range	Mean	Standard Deviation	Median	Q_1	Q_3
Carditis	♂	198	2-45	9.0 ± 0.5	7.1 ± 0.4	8.0	5.5	11.5
	♀	191	2-40	8.6 ± 0.4	5.3 ± 0.3	8.5	6.0	12.0
Valvular lesion	♂	426	1-67	22.9 ± 0.8	15.6 ± 0.5	19.0	10.5	32.0
	♀	460	1-73	23.0 ± 0.7	15.4 ± 0.5	22.0	9.5	32.0
Polyarthritis	♂	682	1-54	13.2 ± 0.4	9.9 ± 0.3	11.0	6.0	17.5
	♀	580	2-52	14.4 ± 0.4	9.7 ± 0.3	12.5	7.0	20.0
Muscle and joint pains	♂	128	2-15	8.7 ± 0.3	3.5 ± 0.2	9.0	6.5	13.0
	♀	153	2-15	9.3 ± 0.3	3.5 ± 0.2	10.5	7.0	13.5
Chorea	♂	132	2-17	8.0 ± 0.3	3.4 ± 0.2	8.5	6.0	11.5
	♀	179	3-19	8.2 ± 0.2	3.2 ± 0.2	8.5	6.5	11.5
Total	♂	1,566	0-67	14.5 ± 0.3	12.2 ± 0.2	11.0	7.0	18.5
	♀	1,563	0-73	15.0 ± 0.3	11.9 ± 0.2	11.5	7.5	20.5

In tables 2 and 3 Q_1 means first quarter and Q_3 third quarter.

DURATION OF DISEASE

In discussing the duration of rheumatic cardiac disease with emphasis on expectancy it is necessary to speak in statistical terms, although a risk is involved. Such terms have unfortunately been the occasion frequently for much misunderstanding, especially among patients and the families of patients, unless the statistical meaning of the figures is carefully explained. It is the meaning of the word "average" which is important. Average

figures are misinterpreted and are taken as applicable to individual cases. Fortunately the outlook is not unfavorable. It is a fact that 10 per cent of patients live for more than thirty years (chart 4, table 3). There are, furthermore, records of survival for at least sixty years. In many cases, probably in most, survival is, however, less long. But even here the account need not be as gloomy as it is often made to appear, for a fourth of the patients live more than seventeen years. Half, however, die within nine years. If the experience is taken as a whole, the mean duration from onset to death is about thirteen years. There seems to be no essential difference between the sexes. The mean duration of life is 12.5 ± 0.3 years for males and 13.0 ± 0.3 years for females, a difference of 0.5 ± 0.37, which lies within the range of chance variation.

DURATION OF DISEASE RELATED TO ONSET

There is a difference in duration of expectancy as related to age at onset. It may be seen (chart 5) that two thirds (65.3 per cent) of the cases begin in childhood, taken arbitrarily to extend from ages 1 to 12 in females and 1 to 14 in males. On further analysis it appears that nearly a third, 31 per cent, of the patients with onset in childhood (20.1 per cent of total) do not survive this age period; that about another third with onset in childhood, 34 per cent (22.5 per cent of total), do not survive adolescence (18 in females and 20 in males), and that early and middle maturity, taken to end in both males and females at 29 and 45, each claims about one sixth, 17 per cent and 13 per cent (11.0 per cent and 8.2 per cent of total); about 5 per cent go on beyond the age of 45.

Sixty-five per cent of cases begin accordingly in childhood and 10 per cent approximately each in adolescence, early maturity and middle maturity. Three per cent begin after 45.

When the onset of disease is in adolescence and early maturity, only about 15 per cent and 19 per cent of the patients do not survive their own age period and in each group there is a relatively large percentage who live even to advanced age.

There is another way of illustrating the phenomena which have just been analyzed (charts 6 and 7). This method is reported also because different presentations impress different people with varying degrees of vividness. In this form of representation 70 per cent of cases among males occur in childhood. Each figure in the chart represents 2 per cent of the total group. Twenty-three figures survive the age period of onset and 12 figures succumb. Twenty-three surviving figures pass on into adolescence. Ten and a half of them go on into maturity; 12½ die. Of the 10½ who go on to maturity only 5½ are alive in middle maturity and 1½ live on into late maturity. Or it may be said that of cases beginning in childhood 66 per cent survive childhood, 30 per cent survive adolescence and 16 per cent early maturity and only 4 per cent go into late maturity. A similar account can be given of the cases which begin in adolescence and in early, middle and late maturity.

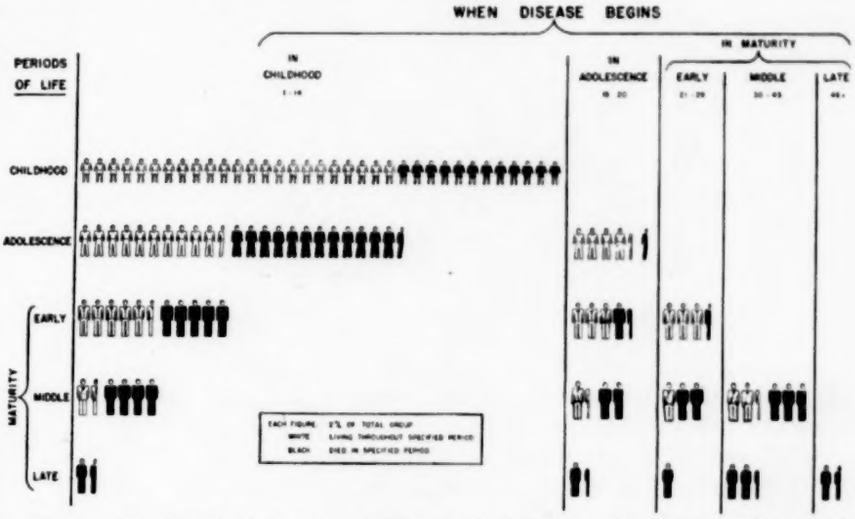

Chart 6.—Duration of life in series of patients with rheumatic cardiac disease (males). Each figure represents 2 per cent of the total group; white indicates patients living through specified period and the black those who died in specified period.

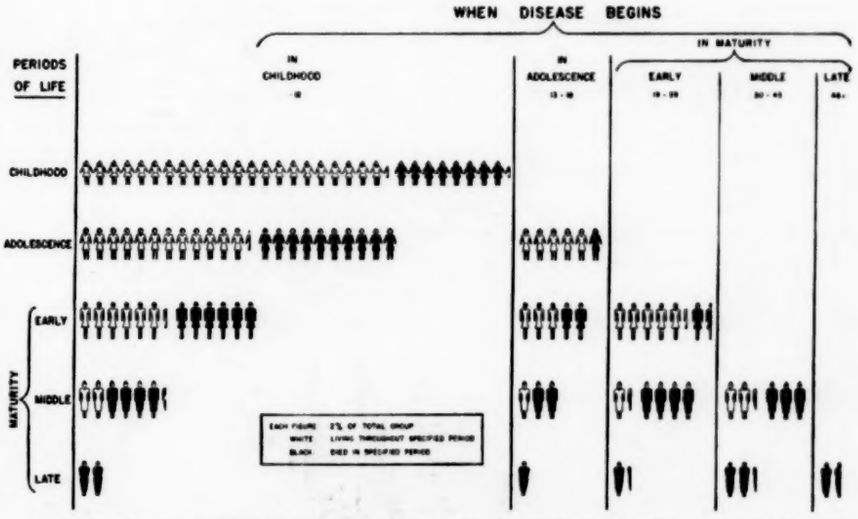

Chart 7.—Duration of life in series of patients with rheumatic cardiac disease (females). The symbols are explained in the legend to chart 6.

A statement almost exactly similar to the one just made for male patients can be made for females except that when the disease is acquired in childhood the survival rate is slightly higher in females. As the age at onset advances, it is somewhat more favorable in males (table 4).

DISTRIBUTION OF CASES AT VARIOUS AGE PERIODS

In any view of the distribution of cases of this disease it is desirable to know the numbers to be found at various age periods (chart 8). From the point of view of one whose experience is gained from life in medical clinics, the result is as follows: Sixty-five per cent of all cases are to be found in childhood. In adoles-

cence are found the survivors of those afflicted in childhood (45 per cent) plus the new cases (11 per cent) occurring, of course, in adolescence. This sum amounts to 56 per cent. The number of cases occurring in adolescence is 9 per cent less than in childhood. In early maturity the number afflicted is 42 per cent, embracing, of course, the survivors from childhood (23 per cent) and adolescence (9 per cent) plus the new cases which occur at this age period (10 per cent). They amount to 42 per cent of the rheumatic population and exhibit a drop of 14 per cent below the number in adolescence. In middle maturity, constituted of the survivors of the first three classes (26 per cent) to which new cases developing in this age period are added, the percentage has fallen another 6, to 36 per cent. Finally, in late maturity, the percentage of survivors from the previous periods (13 per cent) plus the new cases has dropped conspicuously, so that only 16 per cent of all patients with rheumatic fever alive at that time are to be found in this category. It is obvious, therefore, that of the total rheumatic population, the greatest number is found in childhood and that at succeeding age levels the number progressively diminishes, the greatest drops being between adolescence and early maturity and between middle and late maturity. Rheumatic fever, in short, is a disease of childhood and early adult life.

SUMMARY

The method employed by the New York Heart Association for gathering data on the natural history of cardiac diseases and for their subsequent statistical treatment shows the value of statistical technic as a tool in the analysis of clinical medicine, with reference, especially, to the public health.

In this study 3,129 patients with rheumatic cardiac disease have been observed, until death, over a period of fifteen years.

There is no important difference between the sexes in the age at onset. The mean age for males is 14.5 ± 0.3 years and for females 15.0 ± 0.3 years.

Rheumatic fever may begin at any age, but it usually begins in childhood, especially between the ages of 5 and 10 years. At 15, 70 per cent of persons afflicted have already acquired the disease.

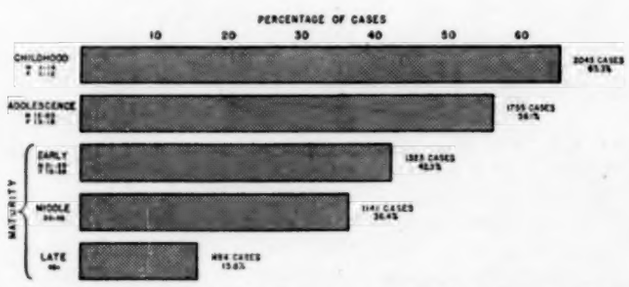

Chart 8.—Rheumatic cardiac disease can be found at all ages. Sixty-five per cent of all rheumatic cardiac disease is found in childhood, less is found in adolescence and still less in each subsequent period of life. The periods of life are specified in the legend to chart 5.

In youth, the onset of the disease is characterized by polyarthritis in about half and by carditis or chorea in about one third. In adult life, the onset is characterized chiefly by polyarthritis and, with advancing age, by the appearance of valvular lesions alone.

The mean duration of the disease is about thirteen years (12.5 ± 0.3 years for males and 13.0 ± 0.3 years for females); 50 per cent of patients die within nine years after onset but 25 per cent live more than seventeen years and 10 per cent for thirty or more years.

There is a difference in duration or expectancy as related to age at onset. When the disease begins in childhood, 69 per cent survive childhood, 35 per cent survive adolescence, 18 per cent reach the age of 30 and 5 per cent go on beyond the age of 45. When the disease begins in adolescence, 85 per cent survive this age period, 55 per cent reach the age of 30 and 21 per cent the age of 46 or more. When the onset is in the twenties 23 per cent and when it is after 30, 44 per cent survive the age of 45.

Of all cases of rheumatic cardiac disease, 65 per cent are to be found in childhood. In the remaining 35 per cent the disease is acquired at later age periods. In adolescence are to be found 56 per cent, the survivors from childhood plus those who have acquired the disease in this age period. In the age group past 45 are to be found only 16 per cent, of whom 13 per cent were first afflicted before and 3 per cent after age 45.

TABLE 3.—*Duration of Illness*

Sex	Number of Cases	Duration in Years: Range	Mean	Standard Deviation	Median	Q_1	Q_3
Males.....	1,566	<1-67	12.5 ± 0.3	10.9 ± 0.2	10.0	5.0	17.5
Females....	1,563	<1-60	13.0 ± 0.3	10.0 ± 0.2	10.0	5.0	19.0

TABLE 4.—*Survival Rate by Sex*

Period of Onset	Sex	Survival Rate Through: Childhood	Adolescence	Early Maturity	Middle Maturity
Childhood.....	Male	66%	30%	16%	4%
	Female	73%	40%	20%	7%
	Total	69%	35%	18%	5%
Adolescence.....	Male	....	89%	63%	26%
	Female	....	83%	50%	17%
	Total	....	85%	55%	21%
Early maturity....	Male	....	....	86%	29%
	Female	....	....	78%	18%
	Total	....	....	81%	23%
Middle maturity...	Male	....	....	....	45%
	Female	....	....	....	43%
	Total	....	....	....	44%

Blind Belief in Laboratory Data.—As one who has taught them [medical students] for many years I can see no change in their ability to learn and hold facts that are new to them; that ability is a quality of the trained mind, and it makes little difference how the mind is trained, whether it be in science, or in the humanities, or otherwise. Indeed, their scientific training may rise to plague them, for it engenders an abiding faith in so-called methods of precision and a blind belief in laboratory data. Just inform the modern student of what the patient complains—never mind about a careful history or physical examination—tell him about the Wassermann, the blood pressure, the blood count, and the urinalysis; give him the results of the stomach wash, the sputum examination, the x-ray of the chest and the gastrointestine series, and the lumbar puncture; let him know what the blood chemistry—including the plasma proteins and the cholesterol—shows and it may not even be necessary for him to see the patient. He will diagnose your case as quickly as did the doctors of a century ago, who in 1832 knew nothing about these tests, and almost as accurately.—Irving, Frederick C.: Safe Deliverance, Boston, Houghton Mifflin Company, 1942.

CHANCROIDAL INFECTION

TREATMENT AND DIAGNOSIS

MAJOR EUGENE GREENWALD
MEDICAL CORPS, ARMY OF THE UNITED STATES

Chancroid, or ulcus molle, is a local, nonindurated, tender ulcer, usually venereal, which is caused by inoculation with Hemophilus ducreyi, a gram-negative bacillus, which appears singly or in short chains and is easily obtainable by smears from the ulcer. It is fairly easy to culture if first innoculated into defibrinated rabbit blood and may then best be grown aerobically on dextrose-cystine blood agar slants.[1]

INCIDENCE

Chancroid is a relatively common venereal lesion and as such presents problems in diagnosis and treatment to the Army Medical Corps. Of its relative incidence during the World War, the Surgeon General Reports show that though it was the least common of the more frequent venereal diseases, comprising 11 per cent of the total, there were 39,044 primary admissions for chancroid in 1917-1918.[2] The calculated noneffective rate was 0.65 per thousand. Its greatest frequency was among Indian and colored troops, being 34.68 per thousand annually.

The rate for enlisted troops in the United States in 1918 was reported as shown in the accompanying table.[3]

Rauschkolb [4] in a civilian clinic found a 66 per cent colored incidence.

The incidence of chancroidal ulcers in females is much less frequent than in the male. Levin [5] believes that the bacillus may exist in the vagina as a nonpathogenic saprophyte, with the female acting as a symptomless carrier of the disease.

A review was undertaken of all cases of chancroidal infection that had been admitted to the Genitourinary Service, Station Hospital, Fort Belvoir, Virginia, from Jan. 1, 1942 to Sept. 1, 1942, a nine month period. At this army post, which is an engineer replacement training center, there is an average normal complement of more than one division. The ratio of colored soldiers to white is about 1 to 5. Analysis of the incidence of Ducrey infection reveals 73 colored to 3 white primary admissions during this period, or a ratio of approximately 120 to 1. This disproportion is not carried over to gonorrhea or to syphilis admissions to as great an extent, though the colored rate for the latter diseases is also disproportionately high.

INCUBATION PERIOD

Following sexual contact a three to twelve day incubation period elapses before the onset of the ulcerations, as generally reported. In the cases which we have observed 18 gave histories of sex contacts twenty-two to ninety days prior to onset of clinical symptoms. Little credence was given to the statements of 14 patients because of low intelligence or apparent unreliability. In the remaining 55 cases the incubation period varied between two and fourteen days.

DIAGNOSIS

Clinically, chancroid infection manifests itself as irregular, nonindurated ulcers with a granular, dirty grayish base, covered with a small amount of grayish purulent discharge. The edges are slightly undermined and irregular. The base bleeds easily on manipulation. The ulcers are more frequently multiple than single, this characteristic apparently being dependent on its autoinoculability. It is therefore to be expected that patients with single lesions have had a shorter period from onset to observation. This was found to hold true in this series. Those with single lesions averaged five to eight days before entering the hospital as compared to 10.4 days in cases in which there were multiple lesions.

Most of the chancroidal ulcers appear at the edge of a phimotic prepuce or, in circumcised males, on the frenum and in the coronal sulcus. These areas are those that are most apt to be traumatized during intercourse. Fifty-four per cent of our patients presented themselves with involvement of the inguinal lymph nodes, which are painful in the more advanced stages and are occasionally associated with constitutional symptoms of fever and anorexia.

The diagnosis of chancroid is not difficult. The clinical picture is fairly typical but should be very carefully differentiated from primary syphilis. It is our procedure to do dark fields on four consecutive days, and only after four negative dark field examinations do we feel justified in ruling out syphilis. In only 2 cases have we, during a subsequent four month observation period, had the serologic test for syphilis become positive. In these cases we had failed to identify Treponema pallidum on repeated dark field examinations.

Rate of Syphilis, Gonorrhea and Chancroid for Enlisted Troops in the United States in 1918

	White	Colored	Ratio W/C
Syphilis	18.83	129.90	1: 6.90
Gonorrhea	78.07	514.68	1: 6.58
Chancroid	4.98	44.5	1: 8.94

In addition to clinical features we have two excellent laboratory aids: the smear and the Ito-Reenstierna skin test. Kornblith and his co-workers [6] in a series of 175 cases reported that the smear was the best single criterion of diagnosis, positive identification being possible in 88.57 per cent of their cases. In our laboratory the smear is stained by the Gram method. However, other workers prefer Wright's stain or methyl green pyronine. We have found these to be relatively simple procedures and very reliable. In our hands the smear was positive in 65 per cent of the cases.

The skin test is without doubt a specific test, as most investigators agree,[7] though there is some disagreement as to the duration of infection before the skin will manifest an allergic response to the antigen. Becker and Obermayer [8] state that five weeks is a minimum time

From the Genitourinary Service, Station Hospital, Fort Belvoir, Virginia.

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8. Becker, S. W., and Obermayer, M. E.: Modern Dermatology and Syphilology, Philadelphia, Montreal and London, J. B. Lippincott Company, 1940, p. 350.

before the skin test becomes positive. Speiser,[9] however, feels that the test becomes positive within six to ten days following the onset of ulceration.

In performance of the skin test we used a commercial antigen,[10] of which 0.1 cc. is inoculated intradermally. It has been our experience that the skin test was positive in 75 per cent of the cases. In the 20 cases in which the test was either negative or doubtful the duration of infection was short. The lifelong character of a positive Ito-Reenstierna test must, however, be kept in mind and, like the tuberculin reaction, a negative test may be as useful as a positive test in the differential diagnosis.

PROPHYLAXIS

Mechanical as well as chemical prophylaxis following sexual intercourse is frequently urged on each soldier. He receives many lectures by medical and line officers and is exposed to training films concerning sex hygiene at frequent intervals. The chemical prophylaxis which is recommended by the Army consists of (1) initial thorough cleansing of the genitalia with green soap, (2) thorough washing of the parts with 1 : 1,000 mercury bichloride, (3) urethral injection of 5 per cent mild protein silver and (4) thorough application of ointment of mild mercurous chloride to the parts.

With this method of prophylaxis we find very few failures with respect to syphilitic or gonorrheal infections. However, chancroidal infections are apparently more resistant and we were much surprised on reviewing our prophylactic failures to observe that a disproportionately large number of these had developed chancroid. Whether this disproportion reflects the more chemoresistance of the organism as compared with the gonococcus and Treponema, whether the prophylaxis is not being adequately applied to the "danger zones" of Ducrey infection or whether this is a chance circumstance in a relatively small number of cases we are not prepared to state. If this experience is generally corroborated throughout the Army, further investigation is indicated.

In our series 38 per cent of the patients had had a chemical prophylaxis, 29 per cent within one hour or less from the time of exposure. This experience is contrary to the experience of most reports. Thomas[11] feels that soap and water thoroughly applied within one hour of the contact is effective. This rate of failure compares very unfavorably to results in gonorrhea and syphilis, in which it comprises no more than 0.8 per cent.

TREATMENT

Until the advent of the sulfonamides the treatment of chancroidal infection was symptomatic rather than specific. During the World War treatment consisted of good local hygiene, under which many chancroids healed spontaneously. However, in progressive cases or very early infections, the thermocautery or the chemical cautery were used with varied success as definitive or abortive treatment. Frequently there was extreme tissue destruction and scarring. In 1918 the average noneffective days or time lost from duty represented 24.9 days.[2]

Since 1918 many therapeutic measures have been recommended, running the gamut from complex mixtures to surgical excision. All of these have been replaced by the sulfonamide drugs, surgery being indicated only when drainage and exposure of the lesion is extremely poor because of phimosis or paraphimosis. The prognosis has undergone a great change in recent years, since sulfonamides have been found useful.[12]

Prerequisite to the intelligent treatment of penile lesions is the recognition of the frequency of mixed infections. It is our practice to search for Treponema pallidum repeatedly in penile lesions subsequent to the positive diagnosis of Ducrey infection, withholding all local therapy until a minimum of four consecutive dark field examinations have been found negative. During this period treatment with sulfathiazole is initiated by mouth. In our experience, often necrotic and heavily secondarily infected lesions become clean and Treponema is then more easily found in the expressed serum.

In this series we have found a chancroidal lesion coincident with syphilis in 10 instances. These cases presented, however, no problem in therapy, for no adverse reaction marked the simultaneous use of sulfathiazole and daily full doses of mapharsen as used in our clinic in the treatment of primary syphilis.[13]

Once the diagnosis of Ducrey infection is made, our routine consists in the administration of sulfathiazole in 4 Gm. daily doses, the initial dose being 2 Gm. The drug is continued in these doses for a minimum of seven days with careful observation for toxic phenomena. In no case in this series was there indication for withdrawal of the drug because of toxicity.

After a minimum of four negative dark field examinations, during which local application of saline dressings was used, the lesions were treated twice daily with soaks of 1 : 8,000 potassium permanganate followed by the application of sulfanilamide powder.

RESULTS

Under this regimen all patients rapidly improved with an average of 7.6 days of time lost from duty. No patient was discharged from the hospital until the lesions had completely epithelized.

Ten per cent of our cases were admitted with fluctuant buboes and surgical intervention was necessary in all of these, since treatment by sulfathiazole alleviated none. In 3 cases it was noted that on admission the nodes were discrete and in spite of favorable response of the ulceration to treatment the nodes went on to suppuration and had to be incised and drained.

There were six recurrences in this series, four of which had received less than seven days of treatment. One of these patients had received only local treatment for five days on his primary admission. Another had a mixed infection with primary syphilis. One case listed as a recurrence was probably a reinfection, since there was a time lapse of ninety-two days between his first and his second admission. On readmission all of these responded well to combined local and systemic therapy as outlined.

It is customary in our clinic to follow all cases of genitoinfectious disease not diagnosed as syphilis by weekly serologic tests for syphilis for one month, and monthly Kahn tests for three months thereafter. However, since this post is a training center, many of the patients are transferred to other stations and field organizations. About 32 per cent of our patients were thus lost. The remaining 68 per cent have remained

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consistently seronegative except for 2, who within four weeks returned with a positive blood test and were subsequently treated for early syphilis. Of these 2 patients 1 had had a negative smear and negative skin test but was repeatedly negative on dark field examination and clinically was considered to have an early chancroidal ulcer. The second patient gave negative smear and positive skin tests and also healed rapidly with sulfathiazole therapy. The diagnosis of chancroid in these 2 cases is open to question despite the fact that the lesions healed without antisyphilitic treatment.

SUMMARY

1. The ratio of colored to white soldiers having Ducrey infection is much higher than the similar ratios for syphilis and gonorrhea.

2. The diagnosis of chancroid is aided by reliable procedures of smear and skin test.

3. Primary syphilis must be carefully differentiated from chancroid by multiple dark field examinations.

4. In our experience, prophylaxis by army routine fails to protect against chancroid as well as it does against syphilis and gonorrhea.

5. Treatment with sulfathiazole in 4 Gm. daily divided doses for seven days is reliable and free of dangerous complications.

CHEMOTHERAPY IN CHILDHOOD SEPSIS

ABRAM KANOF, M.D.
ISIDOR LEBER, M.D.
AND
BENJAMIN KRAMER, M.D.
BROOKLYN

The literature of the past five years has been rich in papers describing all phases of sulfonamide therapy. The pharmacology of these compounds has been ably reviewed by Marshall [1] and by Goodman and Gilman.[2] Long and his associates [3] have thoroughly described the clinical uses and toxic manifestations. In the pediatric literature, Silverman [4] has contributed a critical review of the subject and Bigler and Haralambie [5] have published an exhaustive article particularly excellent for its historic and pharmacologic background.

Very few of these papers have been devoted specifically to the chemotherapy of septicemia. The most complete article is that of Herrell and Brown,[6] which, however, deals with adult cases. Hamburger and Ruegsegger [7] have described 12 cases, and Rammelkamp and Keefer [8] have reported 7 cases of staphylococcemia treated with these drugs. Others who have reported small series of cases of staphylococcic septicemia treated with the sulfonamides have been Thornhill, Swart and Reel,[9] Goldberg and Sachs,[10] Weisman and Russell,[11] Carroll and his associates [12] and Herrell and Brown.[13]

The chemotherapy of pneumococcic septicemia has been described by Dyke,[14] and many such cases were included in the comprehensive report on the treatment of pneumococcic infections in children by Barnett, Hartmann and Perley.[15] No article has been devoted solely to streptococcemia but individual case reports have been plentiful in various articles [16] and in the symposium on the subject which appeared in the *Journal of Pediatarics*.[17]

The present paper is a study of the effects of the sulfonamide drugs on the mortality, morbidity and incidence of septicemia in the pediatric service of the Jewish Hospital of Brooklyn. Since 1937 we have treated 104 patients with the following drugs: sulfanilamide, sulfamethylthiazole, sulfapyridine, sulfathiazole and sulfadiazine. In making this study we have used as controls a series of 320 septicemia patients treated before the advent of the sulfonamides. This older series was shown in an exhibit at the New York Academy of Medicine in 1940. The purpose of our exhibit then was to demonstrate that the prognosis in septicemia depends not only on the infecting organism but also on certain other factors.

FACTORS INFLUENCING OUTCOME

The factors influencing the outcome in septicemia are the age of the patient, the type of pharyngitis accompanying the sepsis, the size of the bacterial invasion, the shift to the left in the count of the polymorphonuclear blood cells, the presence of localizations in certain organs and enlargements and the severity of the particular infection at the time the patient happens to be sick.

We should like to explain what we mean by three of these factors:

1. *Type of Pharyngitis.*—We have placed sore throat, in accordance with its severity, into two divisions.

(*a*) Severe Pharyngitis (pharyngitis predominating or presenting): In this type the throat is acutely and severely inflamed, with the pharyngeal wall and tonsillar fauces severely congested and red at the time that the bacteremia is found.

(*b*) Mild Pharyngitis (pharyngitis nonpredominating, nonpresenting): In this type the throat, though diffusely red, does not appear angry or severely inflamed.

The charts were prepared by Mr. Henry Moore.

From the Department of Pediatrics of the Jewish Hospital.
Read before the Section on Pediatrics at the Ninety-Third Annual Session of the American Medical Association, Atlantic City, N. J., June 10, 1942.

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9. Thornhill, W. A.; Swart, H. A., and Reel, Clifton: Sulfanilamide in Staphylococcus Septicemia, J. A. M. A. **113:** 1638 (Oct. 28) 1939.
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The practical and theoretical implications of this point of view have been discussed in a previous paper,[18] but here it is sufficient to state once more that the type of accompanying pharyngitis has a decided influence on the mortality rate.

TABLE 1.—*Year by Year Mortality in Sepsis*

Year Ending July 31	Death from Staphylococcic Septicemia	Death from Streptococcic Septicemia	Death from Pneumococcic Septicemia
1931	40%	48%	40%
1932	62%	44%	28%
1933	75%	70%	13%
1934	75%	70%	55%
1935	90%	50%	50%

2. *Size of Invasion.*—We should also make clear what we mean by this factor. In a small invasion the broths are positive but the plates remain sterile. In a medium invasion the plates show a growth but there are less than ten colonies per cubic centimeter of blood. If there are more than ten colonies per cubic centimeter of blood on the plates we call it a large or massive invasion.

3. *The Yearly Invasion in the Mortality.*—The importance of this factor is shown in table 1.

Our conclusion at that time was that the gross mortality percentage is not a satisfactory expression of prognosis in septicemia. Study of chart 1, for example, will show that whereas the gross mortality in streptococcemia was 55 per cent, the mortality in certain subgroups was as low as 14 per cent and in others as high as 100 per cent. The gross mortality in pneumococcic sepsis was 46 per cent (chart 2), but some subgroups had a mortality of 16 per cent while other subgroups of pneumococcic septicemia suffered 100 per cent mortality. In staphylococcic sepsis the mortality varied between 23 per cent in one subgroup and 93 per cent in another (chart 3).

In the present paper the results of chemotherapy are analyzed with these principles in mind. The results of treatment will not be presented in terms of gross mortality. Rather, the mortality will be given for each subgroup when treated with sulfonamide and when not thus treated.

CHEMOTHERAPY IN STREPTOCOCCUS HEMOLYTICUS SEPTICEMIA

Chart 1 shows that the use of the sulfonamides has reduced the gross mortality rate to one fifth its previous level. Moreover, it shows that in these 15 treated cases of streptococcemia the difference in mortality between subgroups is still present but that in each subgroup the mortality is less in the sulfonamide treated patients.

Table 2 lists the details of treatment in these cases.

Six of these patients are especially interesting because they are children who probably would have died in the presulfonamide days. Among them were a 3 and a 6 weeks old infant, with streptococcic meningitis and streptococcemia. One of the 2 also showed sacral edema, a finding which, as is shown by chart 1, was invariably fatal. Two other children had lymphatic leukemia with septicemia as a complication. Under chemotherapy, both children recovered from the bacterial invasion; their total white count dropped and the polymorphonuclear cells disappeared. The leukemic picture reappeared when the drug was discontinued. The fifth patient was a 9 month old baby who though he had considerable distention, numerous petechiae and Cheyne-Stokes respirations nevertheless recovered. The sixth recovered despite the presence of pneumonia, pericarditis, considerable distention, hematemesis, icterus and edema of the abdominal wall, forearms and clavicular regions.

Of the 2 children who died, 1 was treated in the early days of sulfonamide drug therapy. He received doses of sulfanilamide which we now consider inadequate, and such complications of the septicemia and pneumonia developed as emphysema, appreciable hepatic enlargement, repeated convulsions, induration of various parts of the skin, considerable distention and cyanosis. The other child who died was a 10 month old baby with pneumonia, mediastinitis and paralytic ileus who was not treated with sulfapyridine until eight hours before his death.

TABLE 2.—*Streptococcemia Treated with the Sulfonamides*

Case	Age	Drug	Administration: Oral	Administration: Subcutaneous	Administration: Intravenous	Highest Blood Concentration	End-Result	Size of Invasion	Drug Reaction	Comment
1	3 wks.	Sulfanilamide	+	0	0	13.5 total	Recovered	Large	Cyanosis	Concentration in cerebrospinal fluid was 5 mg. per 100 cc.
2	9 yrs.	Sulfanilamide	+	0	0	4.5 free 6.0 total	Recovered	Large	.....	
3	4 yrs.	Sulfanilamide	+	0	0	4.5 free 5.5 total	Recovered	Large	Cyanosis	
4	3 yrs.	Sulfanilamide	+	+	0	.....	Recovered	Large	.....	
5	20 mos.	Sulfanilamide	+	0	0	4.1 free	Recovered	Large	.....	Free sulfanilamide; pleural effusion 2.9
6	9 mos.	Sulfanilamide	+	0	0	18.6 free 18.6 total	Recovered	Large	.....	
7	6 wks.	Sulfanilamide	+	+	Into cerebrospinal fluid	.....	Recovered	Small	.....	Meningitis
8	7 yrs.	Sulfanilamide	+	0	0	.....	Recovered	Large	.....	Lymphatic leukemia
9	1 yr.	Sulfanilamide	+	+	0	.....	Died	Medium	.....	Doses very small
10	3 yrs.	Sulfapyridine	+	0	0	12.6 total 9.8 free	Recovered	Small	.....	
11	10 mos.	Sulfapyridine	+	0	0	.....	Died	Large	.....	Died within 8 hours
12	4 yrs.	Sulfapyridine	+	0	+	.....	Recovered	Medium	.....	Also received sulfanilamide into open wound
13	2 wks.	Sulfathiazole	+	0	0	.....	Recovered	Medium	.....	
14	2 mos.	Sulfadiazine	+	0	0	14.0 free	Recovered	Large	Hematuria	
15	4½ yrs.	Sulfadiazine	+	0	+	15.6 total	Recovered	Small	.....	

18. Kanof, Abram, and Kramer, Benjamin: Relation of Sepsis to Infections of the Respiratory Tract, Am. J. Dis. Child. **60**: 1067 (Nov.) 1940.

CHEMOTHERAPY IN STAPHYLOCOCCIC SEPTICEMIA

Chart 3 shows the influence of the sulfonamides on the prognosis in staphylococcemia. Forty-five patients were treated. The gross mortality in this treated series was 46 per cent as against 69 per cent in the untreated patients. Study of this figure leads to certain striking observations applicable to both treated and untreated patients. It shows that some subgroups are affected by chemotherapy while others are refractory to such therapy. These observations may be summarized as follows:

1. The mortality of both treated and untreated patients remained extremely high when there were foci in the bone and viscera.

2. The mortality also remained extremely high in patients who had involvement of the lungs and foci in other viscera.

3. However, when the bone alone was involved the mortality was 23 per cent in untreated patients and zero in the treated group.

4. When the lung alone was involved the mortality was 82 per cent in the untreated and 28 per cent in the treated group of patients.

Chemotherapy reduced the mortality also in those groups of patients with staphylococcemia who had diarrhea. Specific drug therapy was beneficial also in patients under 1 year of age, those having large invasions, abdominal distention, subcutaneous abscesses or pustules or a blood which showed a polymorphonuclear shift to the left and those whose temperature curve was persistently below 103 F.

The patients treated with sulfathiazole or sulfadiazine showed the best results. Twenty-three were treated and 7 (30 per cent) died. Three died soon after admission and before adequate blood concentrations could be established. The only fatality under sulfadiazine therapy was among these 3. The fourth child died with myelogenous leukemia despite sterilizaton of the blood stream. Of the 16 who recovered on sulfathiazole or sulfadiazine therapy, 12 were under 1 year and several had multiple localizations. One was a 5 day old child with icterus gravis neonatorum and omphalitis with septicemia.

The mortality rate was 73 per cent among 15 patients treated with sulfanilamide or sulfapyridine or the two combined. The 4 who did recover had localizations that made for a good prognosis even in the presulfonamide days: 2 had cellulitis, 1 had osteomyelitis and 1 had pneumonia.

The 7 patients treated with sulfapyridine combined with sulfamethylthiazole fared better: 4 recovered. Moreover, all 4 who recovered were under 1 year of age and had a large blood stream invasion. Two of the recoveries were quite dramatic. One occurred in a 6 week old infant who had a large blood stream invasion with multiple lung abscesses and empyema. The other occurred in a 3 day old child with erythroblastosis, pneumonia and staphylococcemia. This child was first treated with sulfapyridine, but the blood did not become sterile until sulfamethylthiazole therapy had been employed.

There were also 2 patients in whom a change from sulfathiazole to sulfadiazine seemed to influence the course of the disease. One was a 10 day old infant with acute pharyngitis, diarrhea and dehydration and generalized furunculosis. He was given sulfathiazole for nine days, but new lesions continued to appear daily and the blood culture remained positive. Shortly after sulfadiazine therapy was begun recovery took place. The second infant, 18 days old, with osteomyelitis of the femur and multiple cutaneous and subcutaneous foci, did not respond to sulfathiazole but recovered promptly after administration of sulfadiazine.

There are indications that the prognosis in staphylococcemia will improve as our experience in the handling of the older sulfa drugs increases and as new drugs of this group are discovered. Chart 4 shows that each year since 1937 the prognosis in staphylococcemia has improved. Of the last 23 patients treated with sulfathiazole or sulfadiazine only 30 per cent died.

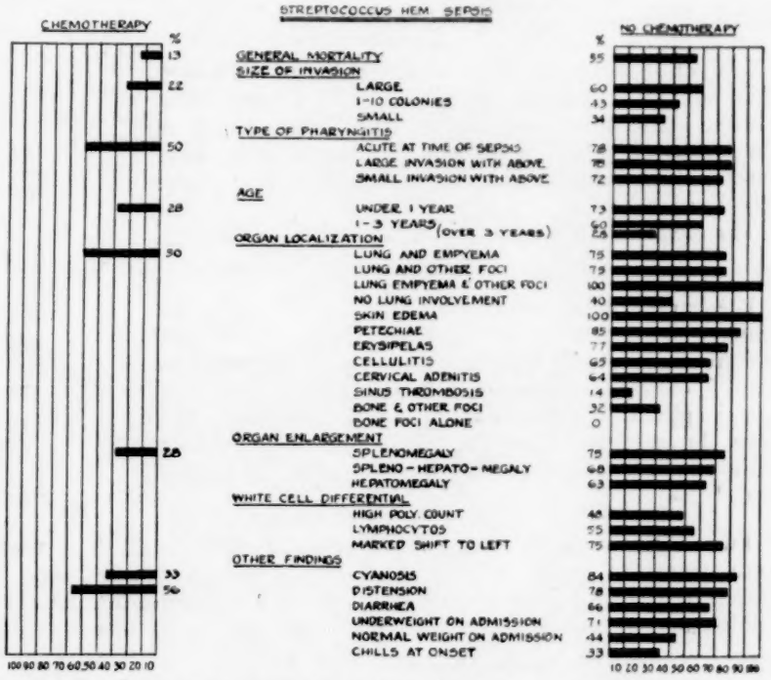

Chart 1.—Factors in the prognosis of streptococcemia in treated and untreated cases. The following factors seem to have no influence on the prognosis: tonsillectomy, loss or gain in weight during illness, previous illnesses, pathologic urinary findings, convulsions (without organic lesions), meningismus, anemia, and type of temperature curve.

CHEMOTHERAPY IN PNEUMOCOCCIC SEPTICEMIA

Chart 3 shows the mortality in pneumococcic septicemia. Sixteen patients were treated with the various sulfonamides. Thirty-one per cent died as against 46 per cent in the group of untreated patients. This does not seem a great improvement until one considers that since the use of the sulfonamides a greater portion of the pneumococcemia patients suffered from large invasions (table 2). Before sulfanilamide, 38 per cent of patients with pneumococcemia had a large invasion. In the present series 68 per cent had a large number of organisms in the blood. Of the pneumococcemia patients with large invasions, 84 per cent died in the presulfonamide era; in the treated series only 25 per cent died.

In chart 2 one sees that only 50 per cent of the patients with severe pharyngitis died, as against 100 per cent in the untreated group. Furthermore, in the

treated series only 1 of 3 patients with erysipeloid or petechiae died, while in the earlier series 89 per cent died. Finally, of 7 patients in the new series who had a shift to the left, only 42 per cent died, while in the untreated series there was a fatal outcome in 67 per cent of the group.

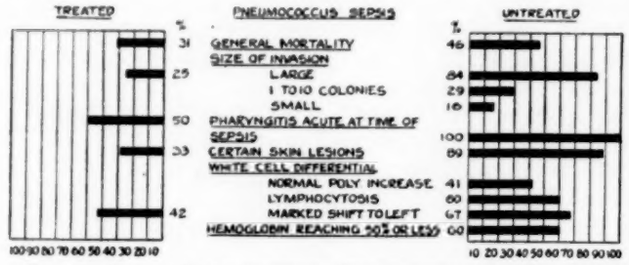

Chart 2.—Factors in the treatment of pneumococcemia. "Certain skin findings" include petechiae, edema, necrosis, erysipeloid, and deep hemorrhages. The lung is so predominantly the localization in pneumococcemia that there are too few cases from which to judge the influence of other types of localization; when such others appear it is usually in association with a large invasion and a fatal outcome. The age of the patient is no factor in the prognosis of pneumococcemia; neither is the state of nutrition, splenomegaly or hepatomegaly, birth weight, previous illnesses, tonsillectomy or pathologic urinary findings.

One of the patients died within twenty-four hours after admission, before the full effect of sulfapyridine therapy could have been established. Two patients in the series who had meningitis died, in contrast with the 2 patients with streptococcemia who survived this complication.

The details of these cases are shown in table 3.

ESCHERICHIA COLI SEPTICEMIA

We have had 8 patients with Escherichia coli septicemia who were treated with these drugs. Three died and five recovered. One of those who recovered was only 5 days old. One was 2 months old and also had Staphylococcus aureus in the blood stream. We have shown that before the sulfonamide era patients with two organisms in the blood stream invariably died.[19]

EBERTHELLA TYPHOSA SEPTICEMIA

Two patients with Eberthella typhosa septicemia were given the benefit of chemotherapy. They were 9 and 10 years of age; 1 died (treated with sulfanilamide) and 1 recovered (treated with sulfapyridine).

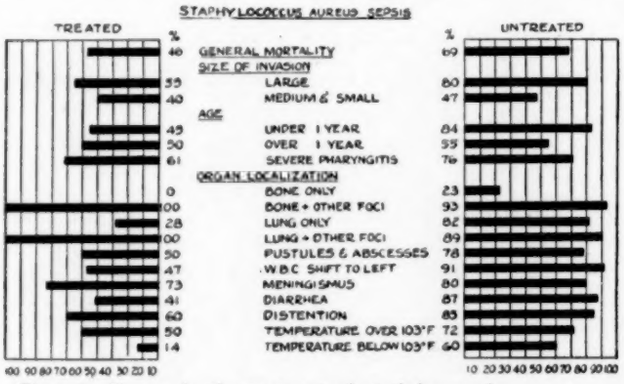

Chart 3.—Factors in the treatment of staphylococcemia.

One patient 2 weeks old with Salmonella paratyphi septicemia died despite treatment with sulfanilamide.

One child aged 10½ years, with Proteus vulgaris septicemia recovered on sulfanilamide therapy. One with Pseudomonas aeruginosa in the blood recovered on sulfanilamide therapy.

A patient aged 18 months with Salmonella typhi murium and Staphylococcus aureus in the blood stream recovered with sulfathiazole and sulfadiazine.

Three patients with Hemophilus influenzae sepsis and meningitis, all about 3 years of age, received sulfanilamide; 2 died and 1 recovered. One patient extremely sick with meningitis and meningococcemia recovered with sulfanilamide therapy.

Two patients suffering from subacute bacterial endocarditis with Streptococcus viridans in the blood died despite treatment with sulfanilamide. One received sulfapyridine in huge doses and 1 received sulfapyridine and sulfadiazine in conjunction with fever therapy. We have had 8 patients with Streptococcus gamma septicemia, but these presented so variegated a clinical picture that we have not attempted to analyze the results. Three of these patients died.

THE EFFECT OF CHEMOTHERAPY ON MORBIDITY

Chart 5 shows the influence of these drugs on the morbidity, as measured by the duration of fever. Of the untreated patients with septicemia who recovered, 80 per cent were sick for more than two weeks and 42 per cent for more than thirty days. Of the treated patients, 30 per cent were sick longer than two weeks but only 6 per cent for more than thirty days.

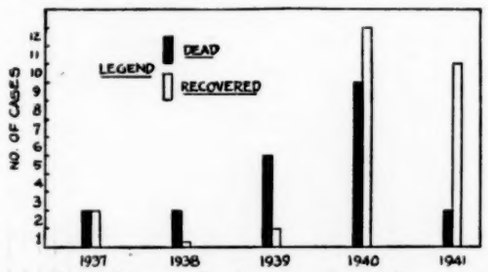

Chart 4.—Improving mortality in cases of staphylococcemia with sulfonamide therapy. Year by year mortality.

ROLE OF THE SULFONAMIDES IN THE PREVENTION OF SEPSIS

The role of the sulfonamides in the prophylaxis of septicemia has been reported in only a few instances. Thomas, France and Reichsman [20] have reported its use in the prophylaxis of rheumatic fever. Gray and Gear [21] found sulfapyridine of some value in reducing the number of carriers during an epidemic of cerebrospinal meningitis, while Hochberg and his associates [22] found it of value in reducing postoperative pneumonia in dogs. Smith [23] found these drugs of no value in preventing acute tonsillitis during an epidemic, though the drugs were of definite value in combating the disease. Hoare [24] did not find them of value in preventing postpartum infections.

We have been interested in the possible effects of the widespread use of the sulfonamides in relatively mild infections on the prevention of septicemia. We have attempted no systematic, citywide survey, but we have relied on tabulations of the incidence of septicemia in proportion to the total number of admissions at the

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24. Hoare, E. D.: The Case for Prophylaxis with Sulfanilamide and M. & B. 693, Lancet **1**: 76 (Jan. 14) 1939.

Jewish Hospital of Brooklyn. This has been done for each type of sepsis for the years preceding and the years following the introduction of the sulfonamide drugs. In addition, we have also studied the differences in the clinical picture of sepsis before and since the use of these drugs in infectious illnesses.

Table 4 shows the yearly incidence of the three major forms of septicemia at the Jewish Hospital since 1931. It shows that from 1937 onward there was a decided drop in the incidence of streptococcus hemolyticus septicemia and pneumococcic septicemia. However, there was no drop in the incidence of staphylococcic septicemia, and in 1940 and 1942 there was actually a rise in the occurrence of this form of sepsis. The table shows that there was no important variation in the total number of pediatric admissions throughout these years.

There have been two important changes in the clinical picture of staphylococcemia as seen in our service since the sulfonamides have been in general use. The first has been a shift in the age incidence. Table 5 shows that before 1938 40 per cent of the patients with staphylococcic bacteremia had been infants under 1 year of age and that 40 per cent had been children over 6 years of age. Since 1938 68 per cent of the cases of staphylococcemia have occurred in children under 1 year, and only 12 per cent in children of school age.

The other variation has been a change in the frequency of certain localizations in this form of sepsis. Before the use of the sulfonamides, 41 per cent of the patients had bone foci and 27 per cent had pulmonary localizations. Since the sulfonamides have been in general use only 16 per cent of the patients have had bone localizations. On the other hand, the incidence of pulmonary localizations has risen to 47 per cent. We have found no change in the incidence of localizations in the skin, peritoneum, intestinal tract, brain or kidneys.

We have also found a change in some of the clinical aspects of pneumococcic septicemia. We [18] reported in the presulfonamide period that in a group of patients we studied 60 per cent of pneumococcic sepsis consisted of a small transient invasion of the blood stream by the pneumococcus in the course of a severe pneumonia. In only 35 per cent of the total was the invasion a large one, with localizations in the meninges, heart or bone. In this group, moreover, the patients were often suffering from a predisposing illness such as chronic glomerular nephritis, congenital heart disease, prematurity or celiac disease. A study of table 3 will show that this particular picture has changed. Among 15 patients with pneumococcemia encountered since the general use of sulfonamides only 2 had pneumonia. Furthermore, 68 per cent of these patients had large invasions in contrast to 38 per cent reported [18] in the presulfonamide era. There has also been a change in the age incidence of pneumococcemia. Table 5 shows

TABLE 5.—*Percentage of Total for Each Organism Occurring in Each Age Group*

Age Group	Before the Use of the Sulfonamides		Since the Use of the Sulfonamides	
	Staphylococcus Aureus	Pneumococcus	Staphylococcus Aureus	Pneumococcus
0 to 1 year	40%	27%	68%	27%
1 to 2 years	5%	14%	10%	27%
2 to 3 years	10%	11%	0	6%
3 to 5 years	7%	11%	10%	40%
5 to 9 years	19%	24%	4%	0
9 to 12 years	19%	11%	8%	0

TABLE 3.—*Pneumococcemia Treated with Sulfonamides*

Case	Age	Drug	Administration: Oral	Administration: Subcutaneous	Administration: Intravenous	Highest Blood Concentration	End Result	Size of Invasion	Type of Pharyngitis	Immature Cells	Drug Reaction	Comment
1	2 mos.	Sulfanilamide	+	0	0	4.1 total 3.9 free	Recovered	Large	Mild	++	0	
2	4 yrs.	Sulfanilamide	+	0	0	7.9 total 6.7 free	Recovered	Large	Severe	++++	0	80% immature polymorphonuclears, 5% mat., 6% lymphocytes
3	3½ yrs.	Sulfapyridine	0	0	+	7.4 total	Died	Large	Mild	++	0	Died in 4 hours of meningitis
4	3½ yrs.	Sulfapyridine	+	0	0	8.7 total 8.3 free	Died	Large	Severe	+	0	Meningitis; blood and cerebrospinal fluid sterilized
5	1 yr.	Sulfapyridine	+	0	+	23.3 total 15.1 free	Recovered	Large	Mild	0	0	
6	4 mos.	Sulfapyridine and sulfanilamide	+	0	0	10.2 free pyr.	Died	Medium	Mild	0	0	
7	3 yrs.	Sulfapyridine	0	0	+	.....	Died	Large	Severe	0	0	Nephrosis, erysipeloid; patient died in 24 hours
8	2 yrs.	Sulfanilamide and sulfadiazine	+	0	+	19.75 total	Recovered	Large	Mild	0	Hematuria	Petechiae purpura
9	6 mos.	Sulfadiazine	+	0	0	8.3 total	Recovered	Small	Mild	0	0	
10	1½ yrs.	Sulfadiazine	+	0	0	9.6 total	Recovered	Small	Mild	0	0	
11	3 yrs.	Sulfadiazine	+	0	0	7.5 total	Recovered	Small	Mild	++	0	Nephrosis
12	1½ yrs.	Sulfadiazine and sulfathiazole	+	0	+	27.4	Died	Large	Severe	++	0	Nephrosis
13	9 mos.	Sulfathiazole	+	0	0	.....	Recovered	Large	Mild	..	..	Osteomyelitis
14	4 yrs.	Sulfathiazole	0	0	+	13.0 total	Recovered	Large	.....	+++	..	Nephrosis
15	2½ yrs.	Sulfathiazole	0	0	+	5.4 total	Recovered	Medium	Severe	0	0	Erysipeloid, nephrosis
16	7 mos.	Sulfadiazine	+	0	0	.....	Recovered	Large	Severe	..	Leukopenia	

TABLE 4.—*Yearly Incidence of Septicemia (1931-1942)*

Year Ending July 31	Staphylococcus Aureus	Pneumococcus	Streptococcus Hemolyticus	Total Cases of Sepsis	Total Admissions to Pediatric Service
1931	5	5	19	39	561
1932	8	7	18	33	765
1933	8	8	27	43	504
1934	4	9	19	32	600
1935	10	20	40	70	504
1936	10	4	16	30	612
1937	9	3	6	18	628
1938	5	3	6	14	574
1939	5	2	2	9	609
1940	23	3	5	31	688
1941	12	3	1	16	558

that before 1938 the cases of pneumococcemia were evenly distributed throughout the years of childhood. Since 1938, however, we have not seen pneumococcemia in children over 6 years of age. This may perhaps be attributed to prompt and effective treatment of children suspected of having pneumonia in this age period.

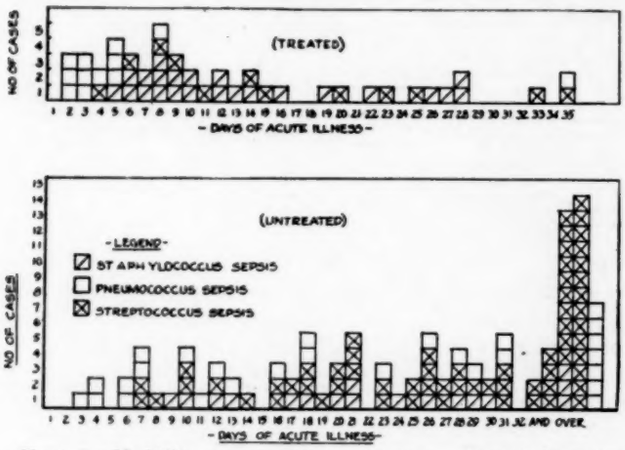

Chart 5.—Morbidity among patients who have recovered from septicemia with and without chemotherapy.

REACTIONS AND BLOOD CONCENTRATIONS

We have encountered only 5 patients who have had an adverse reaction to drug therapy. Two of these had severe cyanosis while being treated with sulfanilamide. Two patients on sulfadiazine therapy developed hematuria. One patient on sulfadiazine therapy developed leukopenia. All these untoward symptoms subsided when the drug was withdrawn.

Chart 6 shows the concentrations of the sulfonamides in the blood reached in the treatment of these patients. Two facts are worthy of note: First, there is no correlation between the concentration of the sulfonamide and the outcome. Second, the highest concentrations were consistently reached when sulfadiazine was used.

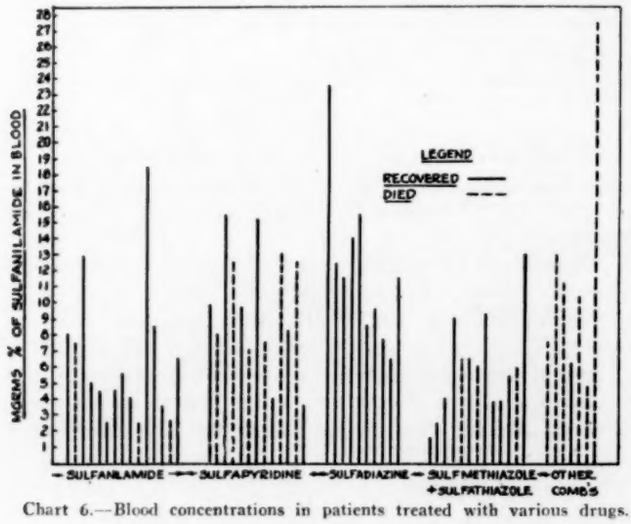

Chart 6.—Blood concentrations in patients treated with various drugs.

COMMENT AND SUMMARY

In this study we have emphasized the importance of certain clinical factors in establishing the prognosis in childhood septicemia. The prognosis in a particular case depends not only on the organism causing the infection but also on the age of the patient, the type of pharyngitis accompanying the sepsis, the size of the bacterial invasion, the reaction of the hemopoietic system as judged by the shift to the left in the count of the polymorphonuclear white cells, the presence of localizations in certain organs and the virulence of the infection in the particular year.

Using as controls a series of patients in whom the influence of these factors was studied in the years previous to sulfonamide therapy, we have established that there is a definite reduction of mortality in patients treated with the sulfonamide drugs. However, there is still a difference in the mortality of different subgroups of the same type of septicemia. We have found, further, that the duration of illness has been sharply reduced in the treated series.

A further finding of importance is that coincident with the use of the sulfonamide drugs there has apparently been a lowered incidence of admissions to our service of patients with pneumococcemia and streptococcemia. Surprisingly, however, there has been no decrease in the frequency of staphylococcic septicemia.

Before 1938 most cases of pneumococcic sepsis presented a bacteremia, transient and small, which was merely an incident in the course of a severe pneumonia. With the use of the sulfonamides, the cases of pneumococcemia which still are seen have most often been represented by severe nonpulmonary infections with large blood invasions and multiple localizations. Moreover, it seems now to have become a disease of infancy rather than an illness of the school age child.

Staphylococcic septicemia has changed in two important respects: Before the sulfonamide period the disease was most often associated with localizations in the bone. Recently this has not been true; the most frequent localizations have been in the lung. A second development has been in the shift of age incidence to the first year of life.

80 Linden Boulevard.

ABSTRACT OF DISCUSSION

DR. REUBEN OTTENBERG, New York: I want to point out the wide variation in mortality from year to year in the statistics. That must warn us to go carefully in interpreting improvement. On the other hand, I have to agree with the general trend of everything Dr. Kanof said. Every one who has used the sulfonamides has found a vast improvement in the results in septicemia due to the streptococcus and to the pneumococcus, and some improvement when it is due to the staphylococcus. The overall reduction in the case of the staphylococcus, as the authors pointed out, is a small figure. A third of the staphylococcus cases were treated with sulfanilamide or sulfapyridine, which we now know are relatively inefficient. In the latter part of the series which, I presume, received sulfathiazole, there was a much better result, and in the cases treated with sulfadiazine there was only one death; it is apparent that the result depends to a considerable extent on the drug. Septicemia is not a single disease; it is a multitude of diseases, all of which are characterized by bacterial invasion of the blood. Before we had the sulfonamides, the most important point in treatment was the eradication of the infecting focus. The introduction of the sulfonamides must not make us omit the attempt to find and remove the focus which is feeding bacteria into the blood. Our failures with sulfonamides were due mostly to the impossibility of finding the focus or of treating it surgically. The fact that frequently today we cure cases without doing anything to the focus should not make us forget that there are still failures with the sulfonamides and that the focus is there. We thought, three or four years ago, that failure was due to inability of the sulfonamides to penetrate the lesion. We now know, as the result of the work of Lockwood and particularly of D. D. Woods of England, that the failure to cure the local lesion is due to the presence of protein breakdown products in the local lesion or possibly, although that has not yet been proved, of para-aminobenzoic acid. The most important observation in

the paper is not the diminished mortality but the diminishing incidence of streptococcic and pneumococcic septicemia in the years since we have had the sulfonamides. Perhaps this is going to be an instance in which the instincts of the general practitioner were right. The experts, for the most part said "You must not give sulfonamides in ordinary ear aches and ordinary sore throats; the danger of hemolytic anemia and agranulocytosis is too great." The general practitioner has gone his way and given the drug to most of these patients. We shall need more evidence, but it looks as though the general practitioner may have been justified.

DR. GEORGE J. BOINES, Wilmington, Del.: About two years ago Dr. Osgood of Oregon suggested that in cases of Staphylococcus aureus septicemia, in which the sulfonamide drug was not effective, recovery might result if neoarsphenamine was added. We had such a case in a boy 12 years of age who had Staphylococcus aureus septicemia and meningitis and the sulfonamide drugs sulfapyridine and sulfathiazole were not effective, but as soon as neoarsphenamine was given along with these drugs prompt recovery occurred. I should like to ask the authors if they had any such cases.

DR. BENJAMIN KRAMER, Brooklyn: Statistically, it is wrong to compare the mortalities of one year with another year and conclude that, because a certain drug has been used, the result is necessarily attributable to the drug. However, the results here in certain groups of cases are so striking that there can be no doubt as to the general effectiveness of these drugs not only in adult sepsis but also in childhood sepsis. One of the particular contributions of this paper is that it calls attention to certain conditions other than specific therapy which influence prognosis and therefore indicates that in any study of the effectiveness of the sulfonamide drugs one has to break down the entire series of cases in order properly to evaluate the effects of treatment. When you do that, it is obvious that there are certain conditions which interfere or completely negate the effects of the treatment. This is important because it constitutes a challenge in that it indicates that the drug itself is not effective, that the drug is not reaching the focus of infection, that the bacteria produce some chemical substance which neutralizes the drug or that some other factor as yet unknown is operating. What some of these factors may be, Dr. Ottenberg has indicated. Another important contribution is the study of the effect on morbidity. This, while it is one of the interesting phases of the paper, is yet one of the weakest, considering the conditions under which we had to work, namely to limit our study to the types of cases admitted to the service, their severity in relation to the total number of cases admitted and to the types of cases previously admitted. However, the results are sufficiently suggestive, perhaps, to warrant a more systematic, more comprehensive and perhaps a better controlled study along the same lines. Anybody who has practiced pediatrics or even medicine in the presulfonamide days and is still active today must realize the striking change in the incidence of certain types of infections. While we have no convincing evidence that the change has been produced by the use of sulfonamide drugs, the evidence that we have is certainly suggestive.

DR. ABRAM KANOF, Brooklyn: Dr. Ottenberg and Dr. Kramer emphasized that there are natural factors which influence the mortality and morbidity. This is the important part of the paper. Just to say that the mortality in staphylococcic sepsis is 60 per cent before treatment and 30 per cent after treatment does not tell the story. It varies without sulfanilamide or sulfathiazole from year to year, and with different subjects, and that is a point which we wanted to emphasize. Dr. Ottenberg brought up the question of multiple blood stream invasions. Dr. Kramer and I reported a series of cases of multiple blood stream invasions about six months ago and classified multiple blood stream invasions into four groups. In the first group one gets two organisms in the same culture. In our experience, those cases were invariably fatal. In our second group there is one organism on one occasion and another one in a subsequent culture. For example, one may see a youngster who has a staphylococcic septicemia, who goes along for three or four weeks, has an occasional positive staphylococcus blood culture and then suddenly develops an erysipeloid rash, and one takes a blood culture and finds a hemolytic streptococcus. Most of those patients died, although some recovered. A different type of multiple blood stream invasion is one in which a variant of the first organism appears in a subsequent culture. One may have a patient with a Streptococcus hemolyticus septicemia who shows two or three positive cultures with that organism. Then one day a culture of the blood reveals Streptococcus viridans or gamma streptococcus. Those are also considered multiple blood stream invasions, but they usually end in recovery. The fourth is the type in which the second organism is a casual invader. A youngster has a positive typhosus in the blood on one or two occasions and then when nearing convalescence one finds that he has a gamma streptococcus in the blood. In the first group, in which there are two organisms in the same blood culture, the patient invariably died before the era of the sulfonamides. Now we have 2 such patients who recovered on sulfathiazole.

TESTOSTERONE PROPIONATE PELLET IMPLANTATION IN GYNECIC DISORDERS

ROBERT B. GREENBLATT, M.D.
AUGUSTA, GA.

The employment of so-called "male" sex hormone in the treatment of certain gynecic disorders may appear paradoxic but it is not unphysiologic. Androgenic hormones are not peculiar to the male, for they are elaborated also by the female. The Callows,[1] Womack and Koch[2] and others have isolated from the urine of normal women the same two androgens identified in the urine of normal males. It is reasonable to suppose that in woman's hormonal economy androgens play some physiologic role.

In recent years there has been an increasing trend to use androgens in gynecologic therapy. This practice has received much support, much condemnation. The schism is wide. Two diverse opinions, each crystallized from a wealth of experience, are found in the statement of Geist and Salmon[3] that "the use [of androgens] as therapeutic agents has a sound rationale" and the contention of Hamblen[4] that "androgens have no place in rational gynecologic therapy."

A rapidly accumulating literature has established many therapeutic uses for these steroids in woman.[5] The parenteral, oral or percutaneous route of administration may require massive doses to assure therapeutic results, and this may not be attended always by balanced physiologic reactions. It must be admitted that after large parenteral doses (500 mg. a month) undesirable side reactions such as temporary or permanent virilism may develop.[6] Such doses used parenterally have

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From the Department of Experimental Medicine, University of Georgia School of Medicine.

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Read before the Section on Obstetrics and Gynecology at the Ninety-Third Annual Session of the American Medical Association, Atlantic City, N. J., June 10, 1942.

The pellets of testosterone propionate used in this study were furnished by Ciba Pharmaceutical Products, Inc. Drs. E. Oppenheimer and R. A. MacBrayer cooperated and gave suggestions.

1. Callow, N. H., and Callow, R. K.: Isolation of Androsterone and Transdehydro-Androsterone from Urine of Normal Women, Biochem. J. **32:** 1759 (Oct.) 1938.

2. Womack, E. B., and Koch, F. C.: Testicular Hormone Content of Human Urine, Endocrinology **16:** 273 (May-June) 1932.

3. Geist, S. H., and Salmon, U. J.: Androgen Therapy in Gynecology, J. A. M. A. **117:** 2207 (Dec. 27) 1941.

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5. Salmon, U. J.: Rationale for Androgen Therapy in Gynecology, J. Clin. Endocrinol. **1:** 162 (Feb.) 1941.

6. Greenhill, J. P., and Freed, S. C.: Virilism in Women Caused by Androgenic Therapy for Menstrual Disturbances, J. A. M. A. **112:** 1537 (April 22) 1939.

given cause for protestation that androgens are contrasexual. It may well be that the dose and not the hormone is contraphysiologic.

It has been noted by many investigators[7] in both animal experimentation and clinical investigation that implantation of pellets of crystalline steroids results in

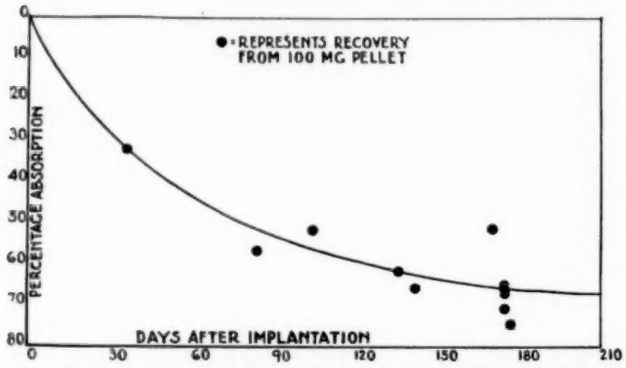

Fig. 3.—Percentage absorption curve for 100 mg. pellets of testosterone propionate obtained by plotting percentage absorption of eleven pellets recovered at intervals varying from thirty-six to one hundred seventy-seven days.

a slow and more physiologic absorption of the substance than that observed after parenteral administration. Since the amount of hormone released to the organism is continuous though minute in quantity, it is conceivable that by this method all the beneficial effects of larger doses of androgens may be obtained without the arrhenomimetic phenomena. This paper deals with my observations following the implantation of pellets of testosterone propionate for the therapy of various gynecic disorders.

MATERIAL AND METHODS

Sixty-four women ranging in age from 19 to 53 had pellets of testosterone propionate implanted subfascially. From 1 to 4 pellets were implanted at one time. The pellets varied in weight from 22 mg. to 200 mg. Though the average dose was about 100 mg., nevertheless as little as 22 mg. and as much as 400 mg. was employed. Sixty-eight implantations were performed on 64 patients, of whom 61 had but one implantation. One patient had three and 2 had two implantations. Studies were conducted on patients presenting a variety of gynecic disorders, namely functional uterine bleeding, uterine fibromyomas with or without menstrual disturbances, dysmenorrhea, menopausal syndrome and nervous tension states. Attention was given to coincident disturbances of micturition and the status of the patient's sexual libido before and after implantation.

Vaginal smears, endometrial biopsy studies and blood chemistry determinations were obtained in the majority of cases before implantation and were repeated at various intervals after implantation. Many vaginal biopsy studies were also taken before and after implantation. The patients were seen, as a rule, at weekly to monthly intervals and have been under observation from four to twenty-two months.

PROCEDURE

All implantations were made under sterile conditions in the operating room. The skin of the abdomen was prepared and then an area between the pubis and the umbilicus 3 cm. long was infiltrated with 1 per cent procaine hydrochloride down the midline to the rectus sheath. An incision was made through the skin and subcutaneous fat and the rectus sheath was visualized. A small incision was made in the sheath exposing the rectus muscle. The pellet, or pellets, were then inserted under the sheath to lie on top of the muscle belly. The fascial sheath was closed with No. 1 chromic catgut and the skin and subcutaneous fat approximated by silk stay sutures.

FUNCTIONAL MENOMETRORRHAGIA

Eight patients with severe functional menometrorrhagia of from three months' to two years' duration had submitted to curettage and/or a variety of therapeutic procedures with disappointing results. Implantation of testosterone propionate pellets in doses varying from 96 to 205 mg. was soon followed by cessation of bleeding in every case (fig. 7). It is noteworthy that in 5 of the patients bleeding was known to be associated with cystic glandular hyperplasia or persistent estrogenic endometriums. In 3 cases, in spite of the control of flooding episodes, repeated suction curettages revealed persistent hyperplasia or estrogenic endometriums for many months after pellet implantation. Stabilization of the menses was the rule, though temporary cessation of the menses or an increase in the interval between periods frequently occurred. In 2 cases menorrhagia was associated with an imperfect progestational endometrium. Following implantation normal cyclic bleeding occurred from an improved progestational endometrium. Two patients with menorrhagia not benefited by this procedure were excluded from this group because of concomitant pelvic inflammatory disease.

MENOMETRORRHAGIA ASSOCIATED WITH UTERINE FIBROIDS

Twelve patients with severe menometrorrhagia associated with uterine fibroids had been hospitalized but were considered poor risks for major surgery. Pellets of testosterone propionate were implanted in doses of

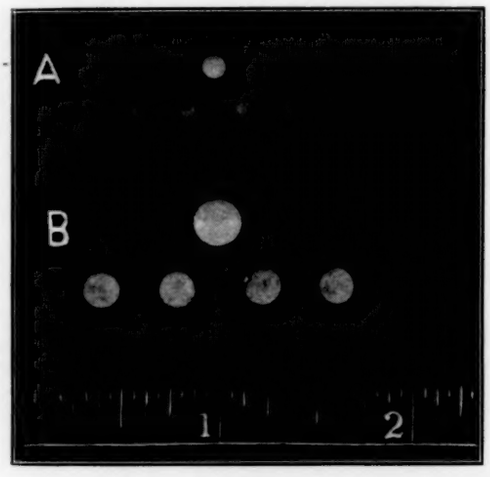

Fig. 5.—Compare original size pellet with size of recovered pellets: *A*, four 25 mg. pellets recovered one hundred and thirty-three days after implantation. *B*, four 100 mg. pellets recovered one hundred and seventy-seven days after implantation.

from 25 to 302 mg. Subsequently, though the degree of flooding was less in all but 1 case, nevertheless the results were very poor in 3 cases (8, 9, 11) and hysterectomy was performed six to seven months later. Of the 3, 2 presented submucous fibroids and 1 multiple fibroids with pelvic inflammatory disease. In a fourth

7. Deansley, R., and Parkes, A. S.: Factors Influencing the Effectiveness of Administered Hormones, Proc. Roy. Soc. London, S. B. **124:** 279, 1937. Thorne, G. W.; Howard, R. P.; Emerson, Kendell, Jr., and Firor, W. M.: Treatment of Addison's Disease with Pellets of Crystalline Adrenal Cortical Hormone (Synthetic Desoxycorticosterone Acetate) Implanted Subcutaneously, Bull. Johns Hopkins Hosp. **64:** 339 (May) 1939.

(case 7) there was moderate improvement in the degree of menorrhagia for thirteen months; then bleeding episodes began to recur. In the remaining 8 cases satisfactory alleviation resulted, and in some of these for as long as eighteen to twenty-two months. Testosterone propionate pellet implantation proved of value as a

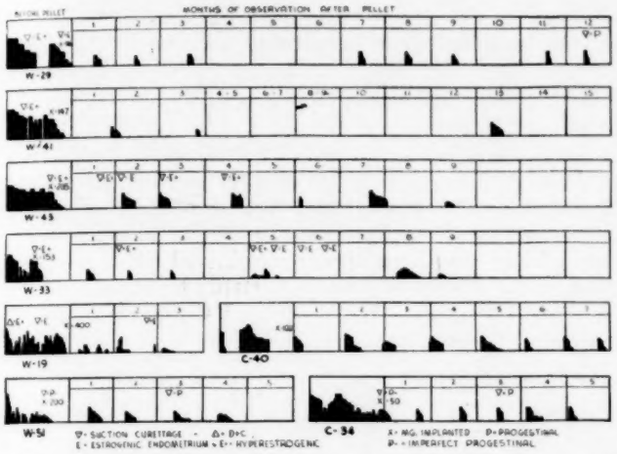

Fig. 7.—Influence of implanted pellets of testosterone propionate on 8 patients with functional menometrorrhagia.

temporary measure, affording an opportunity for enough improvement in the patient's physical condition to permit ultimate major surgery (cases 3 and 12). It was not meant as a substitute for surgery. The endometrial studies in case 5 are of interest, for this is the only instance in the series in which testosterone propionate pellets suppressed further ovulation. The patient was 45 years of age and had flooded for two to three weeks in every month for about two years. At the time of implantation of a 100 mg. testosterone propionate pellet, suction curettage revealed an imperfect progestational endometrium. One month later she bled from a progestational endometrium. Thereafter the interval between the menses increased and repeated suction curettages at various intervals revealed an estrogenic or hypoestrogenic endometrium. She has not menstruated in the past year. This may be coincidental. On the other hand, this may be an example of premenopausal bleeding being tided over a crucial period by pellet implantation (fig. 8).

HYPERMENORRHEA-POLYMENORRHEA

Hypermenorrhea or polymenorrhea occurred in 18 cases, in eleven of which there were uterine fibroids. In 7 the disturbance was functional. Testosterone propionate pellet implantation proved of value in ameliorating this disturbance in the functional group and in all but 2 of the group with uterine fibroids. Of these 2, 1 was temporarily alleviated and in the other the pellets sloughed out shortly after implantation.

UTERINE FIBROIDS WITHOUT MENSTRUAL DISTURBANCES BUT WITH PELVIC DISCOMFORT OR DEBILITY

Pellets of testosterone propionate were implanted in 7 patients because of massive uterine fibroids. These patients were anemic and complained of pelvic discomfort, general weakness and pressure symptoms. As a rule, following pellet implantation these patients felt stronger, pelvic discomfort was lessened and the anemia showed some improvement. Within a few months many of the patients with uterine fibroids in this and the other groups volunteered the fact that they were certain that regression in size of the tumor had occurred. Subjectively there was recession of the level which the tumor had gained. Respiration was easier when the patient was reclining, and the girth of the abdomen decreased (the belts on their dresses served as a measure) in spite of a moderate gain in weight. Objectively it was felt that, with the exception of 2 cases, there was a definite decrease in the size of the palpable tumors.

MENOPAUSE

Eight women in this series had pellets of testosterone propionate implanted for the amelioration of the menopausal syndrome (table 2). It was found that the best results were obtained with large doses, and the patient who responded most satisfactorily was one in whom four 100 mg. pellets had been implanted (case 8). This patient had been treated with estrogens for some fifteen months with satisfactory though transitory results requiring continuous therapy. Another patient (case 5) required 5 mg. of estradiol dipropionate parenterally every two weeks to keep her free from the hot flashes that kept her awake at night. With the implantation of two 200 mg. pellets of testosterone propionate she has remained reasonably free from her menopausal syndrome for the seven months since their implantation.

DYSMENORRHEA

Nine women with functional dysmenorrhea were selected for pellet implantation because of the severity of their symptoms. On each patient various therapeutic procedures had been tried with disappointing results. Physicians had suggested hysterectomy or presacral nerve resection to 5 of these patients. The patients

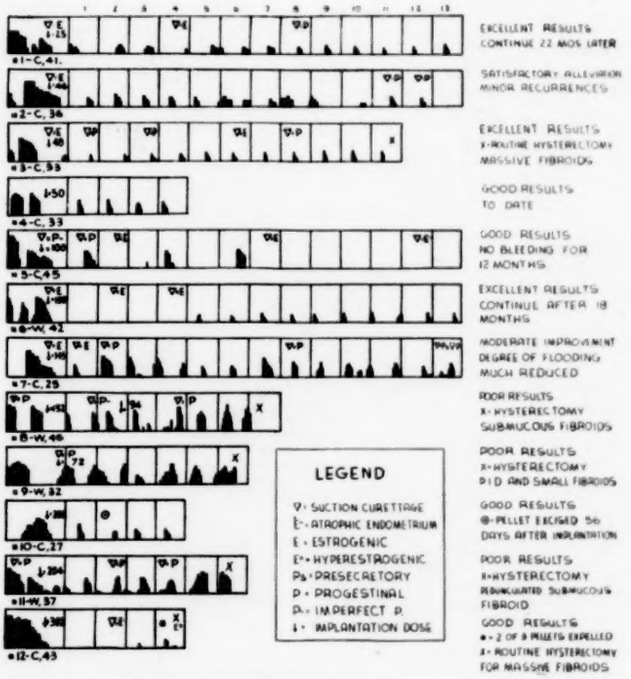

Fig. 8.—Influence of implanted pellets of testosterone propionate on menorrhagia associated with fibromyomas in 12 cases.

ranged in age from 19 to 38 years and the dose of the pellets implanted in each varied from 150 to 400 mg. No decided disturbance in the regularity of the cycles occurred in spite of the fact that two 200 mg. pellets were implanted at one time in 5 of the patients in this group. In 1 patient extrusion of the pellets occurred thirty-six days after three pellets totaling 200 mg. had

been implanted. She experienced satisfactory alleviation of pain during the menses while the pellets remained in situ, and only that period was included in the statistical data. Of the observations noted on forty consecutive cycles it was found that 75 per cent relief or better was obtained in 48 per cent of the cycles and approximately 50 per cent relief followed in 27 per cent of the cycles. Results were unsatisfactory in 25 per cent of the cycles. In another group of 14 patients whose dysmenorrhea was not primary or functional but associated with uterine fibroids, the results appeared to be better. These patients were observed from eight to twenty-two months, a much longer period than for the group with functional dysmenorrhea. In 11 patients the pain was considerably ameliorated. In several there were recurrences after variable lengths of time coincident with absorption of the greater part of the implanted pellet.

INFLUENCE OF TESTOSTERONE PROPIONATE PELLET IMPLANTATION ON NOCTURIA

In the group of women under consideration it was noted that many of them had coincidental disorders of micturition to which no pathologic basis could be ascribed. Thirty women had uterine fibromyomas and in 19 instances nocturia of two to ten times a night was present. Frequently diurnal frequency and dysuria were associated with the nocturia. After pellet implantation there was partial to complete amelioration of this syndrome. Because of this observation it is felt that the belief perpetuated in textbooks and in teaching may well be fallacious—that nocturia associated with uterine fibromyomas is due to pressure on the bladder.

In another group of 10 women with stigmas of endocrine imbalance, such as functional menorrhagia (5 cases), the menopause (4 cases) and dysmenorrhea (1 case), there was a similar syndrome of nocturia with or without diurnal frequency or dysuria. Routine urinary findings were negative or of little significance. The syndrome was partially or wholly alleviated following pellet implantation. Of the remaining 34 patients in this series without urinary disturbances, nocturia developed in 2 following pellet implantation (fig. 9).

LIBIDO

Information as to the status of the sexual libido before and after implantation was obtained from 54 women. The patients were classified as follows: (*a*) 8 women who never had any libido or had very little of it; (*b*) 22 women who had once known libido but lost it; (*c*) 14 women who had a moderate amount of libido, and (*d*) 10 women in whom libido was good or very good.

It was impossible to increase the libido of 2 psychologically frigid women who never had experienced sexual desire. On the other hand, restoration of the libido readily occurred following implantation in those women who at some time had known libido. Many married women volunteered the information that their loss of sexual desire led to marital discord. Following pellet implantation there was a return of coital pleasure which often terminated in orgasm. A reawakened interest on the part of the husband usually followed and husband and wife once more fell in love. Among those women who had a strong to moderate degree of sexual desire before implantation, all noted either no significant change or further increase in sexual pleasure. Two women with normal libido had a temporary decrease in sexual desire for several weeks immediately after pellet implantation and then a resurgence of the libido to a greater degree than that before the implantation. In several instances it was noted that the libido returned to the preimplantation status by the end of the third to the eighth month. In the majority, however, it persisted long after the pellets had been absorbed.

BLOOD CHEMISTRY STUDIES

Before pellet implantation and at various intervals afterward blood samples were taken and quantitative analyses were made of the following components: Non-protein nitrogen, sugar, uric acid, creatinine, sodium, potassium and calcium. Although the values obtained fluctuated for each individual sample from the same patient and from different patients, there was no decided deviation from the normal fluctuations. The clinical picture observed before and after implantation of testosterone propionate pellets cannot be ascribed to any disturbance of those constituents of the blood that were studied, since the blood analyses showed them to be within the limits of normal values. On the other hand, Albright [9a] has shown that testosterone propionate is capable of restoring and maintaining a positive nitrogen balance, and promoting phosphorus and some calcium retention.

ENDOMETRIAL STUDIES

In 39 cases of this series endometrial biopsies were available for study. In the larger number of these there had been at least one biopsy made before pellet implantation and from one to seven afterward. After pellet implantation biopsies were usually done on the first day of the menses and as close to the expected onset of menses as possible. Occasionally biopsies were done in midcycle or during an amenorrheic episode to study the effect, if any, of the implanted pellet on the endometrium. The biopsy specimens were stained routinely with hematoxylin and eosin, and frequently alcohol fixed tissue was subjected to Best's carmine stain and rechecked by the iodine reaction for glycogen.

TABLE 2.—*Influence of Pellet Implantation on Menopausal Syndrome* *

Case	Race	Age	Dose, Mg.	Menopause	Before Pellet	Months Observation After Pellet							
						1	2	3	4	5	6	7	8
1	W	30	75	Post radiation	+++	+	—	—	—	—	+	++	++
2a	W	29	98	Post radiation	++++	—	—	+	++	+++	+++	+++	..
2b	W	29	200	Post radiation	+++	—	—	—	+	++	+++	..	..
3	W	29	66	Castration	+++	—	—	—	—	..	..	..	..
4	W	29	50	Castration	++	+	—	—	—	—	—	—	—
5	W	37	400	Castration	++++	+	±	±	+	+	+	±	..
6	W	53	75	Natural	++++	—	—	—	+	++	+++	++++	..
7	W	50	98	Natural	+++	++	+	+	++	++	+++	++++	..
8	N	42	400	Natural	++++	+	±	±	±	—	—	—	..

* —, satisfactory alleviation; ±, occasional hot flashes; +, mild; ++, moderate; +++, severe; ++++, very severe.

9a. Albright, Fuller; Parson, William, and Bloomberg, Esther: Therapy in Cushing's Syndrome, J. Clin. Endocrinol. **1**: 375 (May) 1941.

An analysis of the histologic studies of these biopsy specimens permits of an answer to the obvious query What is the effect of implantation of testosterone propionate pellets on the endometrium of the adult woman? In general, implantation of pellets in doses up to 400 mg. of testosterone propionate does not interfere with development of progestational endometrium in the woman with a normal cycle. Moreover, in some cases pellet implantation enhanced the development of a more mature progestational endometrium in the women who had previously bled from an imperfect progestational endometrium.

On the other hand, it appeared that testosterone propionate in doses used in this study was capable of maintaining the endometrium in the status attained before the implantation. For instance, cystic glandular hyperplasia or a persistent estrogenic endometrium was maintained in the majority of cases for many months after pellet implantation. It might be argued that such a finding is proof of the ineffectiveness of the hormone. The clinical improvement of the patient precludes such a conclusion. Furthermore, in many instances the anovulatory bleeding episodes were stabilized and bleeding recurred cyclically from a progestational endometrium. In only 1 case, and that in a woman aged 45, did suppression of ovarian function occur as reflected in the endometrial pattern. This incident may have been in consonance with the hypophysial gonadal relationship expected at or near the menopause. The continuous and gradual absorption of androgenic substances from the testosterone propionate pellets implanted in doses up to 400 mg. does not inhibit the rhythm of hypophysial activity. Fresh corpora lutea were often observed in patients submitted to laparotomy (hysterectomy) several months after pellet implantation. Furthermore, interference with glycogen deposition in the secretory endometrial glands was not found.

VAGINAL SMEARS AND VAGINAL MUCOSA

Routine vaginal smears were taken before implantation and at frequent but irregular intervals after implantation. The smears were stained routinely by carbol fuchsin and occasionally by the Shorr technic. The vaginal p_H was determined by the use of nitrazine paper and a routine study of the vaginal secretions was made in search of monilia or trichomonads. Vaginal biopsy specimens were taken in many cases before implantation and at various intervals after implantation. In general, pellet implantation in the dosages employed did not interfere with the deposition of glycogen in superficial layers of the vaginal mucous membrane in those with functional ovaries (fig. 10). Occasionally temporary regression of the vaginal mucosa exhibiting castration effects (fig. 11*A*) were noted soon after implantation, but maturation toward normal (fig. 11*B*) soon followed. In castrate or menopausal patients with moderately mature vaginal smears, pellets of testosterone propionate in small or moderate doses did not suppress or enhance the maturation of the vaginal epithelium. In 2 menopausal patients with castrate smears in whom larger doses (400 mg.) were employed it was noted that testosterone propionate had an estrogenic effect, maintaining on the average a 3 plus reaction. In the menopausal cases with castrate smears similar estrogenic effects were not observed when smaller doses were employed.

ARRHENOMIMETIC PHENOMENA

Arrhenomimetic phenomena were not observed in any patient in this series. Particular attention was given to the patients as to changes in voice, hirsuties and enlargement of the clitoris. In spite of the fact that some patients had a moderate degree of masculine crines before implantation no further exaggeration of hairy distribution was noted following pellet implantation. Many patients felt that their voices were stronger and sang with more resonance. Definite lowering of the pitch or persistent hoarseness was not observed. Slight hypertrophy of the clitoris was noted in but few patients and in none was there pathologic enlargement.

MISCELLANEOUS OBSERVATIONS

In general, patients experienced a sense of well-being and increased strength. They did not fatigue as easily. Appetites were better. In patients under observation

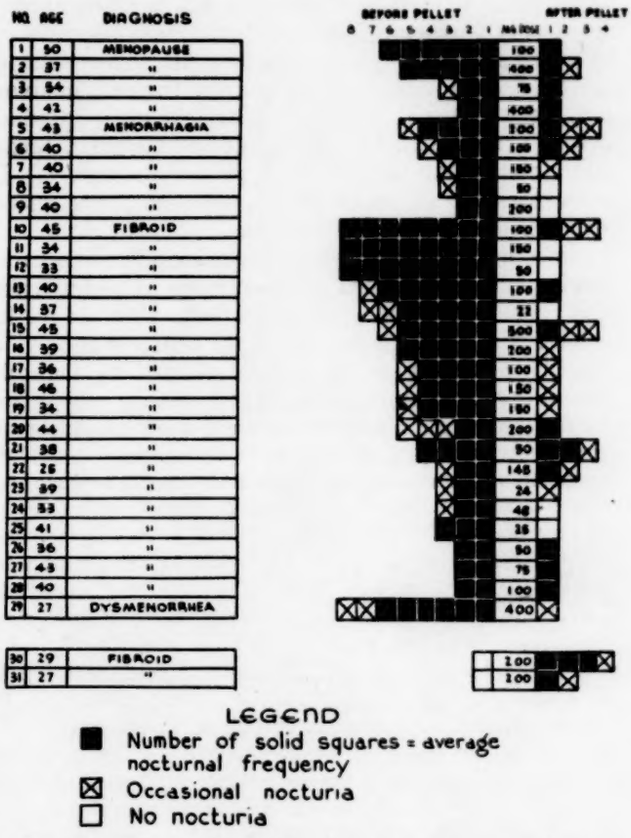

Fig. 9.—Influence of implanted pellets of testosterone propionate on nocturia.

from four to twenty-two months an increase in weight of 1 to 20 pounds (453 Gm. to 9.1 Kg.) was noted. Blood pressure values remained stationary. Some of the patients with menstrual migraine noted diminution in the frequency and severity of attacks. Premenstrual tension was diminished when a smaller dose (150 mg. or less) was used but was noted occasionally with larger dosage. Patients with premenstrual mastalgia and lumpiness of the breast obtained relief in all but a few instances. Nausea and vomiting associated with severe functional dysmenorrhea was arrested. Dyspareunia due to dryness of the vagina was partially alleviated because of increased mucoid vaginal secretions following pellet implantation. Pain or induration at the site of implantation occurred when in some instances one

or more of the implanted pellets were extruded from their subfascial locus and were harbored in the subcutaneous fat.

COMMENT

There is no way to study human physiology other than to study human beings. Present concepts of the physiologic role played by androgens are based on the antigynecogenic responses obtained through the employment of massive and probably unphysiologic doses. The voices that have been raised against the use of androgens in female patients result from the concept that gonadal hormones should be sex specific, as well as on the observation that defeminizing and "ovarian-negating" effects are produced by androgens following massive parenteral doses. The parenteral use of massive doses of testosterone propionate in the female is contraphysiologic and "ovarian negating"; however, the use of comparatively large doses of estrogens is also "ovarian negating." It must be recognized that in many aberrations of gynecic function the therapeutic effectiveness of androgens cannot be matched by the employment of estrogens. Moreover, some women respond unfavorably to estrogenic therapy. Estrogens may produce severe nervous tension states, uterine bleeding, breast pain, abdominal bloating and pelvic discomfort. In such cases androgens frequently yield gratifying results without undesirable side reactions.

Since it has been shown by Deansley and Parkes that the implantation of hard pellets permits of a continuous and prolonged hence nearly physiologic action of the fat soluble hormones, it was felt that the action of androgens in female therapy might best be studied by the subfascial implantation of pellets of testosterone propionate. In this way more nearly physiologic doses of androgens would be employed and some of the complex biologic properties of testosterone propionate might be clarified. Since arrhenomimetic phenomena were not observed in any one of the 64 patients in this series by the use of subfascial implantation of testosterone propionate pellets in doses varying from 22 to 400 mg., a reconsideration of the physiologic properties of testosterone propionate thus employed might be in order.

The doses used in this therapeutic venture were at first and perhaps still are empiric. In March 1941 we recommended implantation of pellets in doses from 22 to 145 mg. of testosterone propionate for the palliative therapy of uterine bleeding associated with fibromyomas.[8] The doses were gradually increased to insure therapeutic effectiveness in patients with dysmenorrhea and menopausal syndrome. Virilism was not observed with doses up to 400 mg. Larger doses were not used, since Loeser[10] had implanted with therapeutic effectiveness testosterone and testosterone propionate pellets in doses of 600 to 1,650 mg. but observed transitory signs of masculinization in every one of 8 patients in his series. Geist[11] implanted pellets containing from 150 to 500 mg. of testosterone propionate subcutaneously in 9 cases (8 with functional bleeding and 1 with menopausal syndrome) and reported in February 1941 that he found no therapeutic effect or evidence of effective absorption. It is difficult to reconcile this observation with a later opinion expressed in June 1941 by Geist and Salmon[3] that androgens administered by subcutaneous pellet implantation in doses of 50 to 675 mg. were now believed to be therapeutically effective but that arrhenomimetic symptoms followed after a few weeks. Abarbanel[12] and Geschickter[13] have used testosterone propionate pellets in much smaller doses with satisfactory results.

An evaluation of my results indicates that testosterone propionate pellet implantation is capable of alleviating many aberrations of gynecic function without suppression of hypophysial gonadotropic function or interference (antagonism) with the action of endogenous estrogen or progesterone on the uterus and vaginal mucosa. Ovulation and cyclic maturation with glycogen deposition of both the secretory endometrium and the vaginal mucosa was not interfered with. Experimentally, Hartman[14] made similar observations on the endometrium of the monkey. In menometrorrhagia the therapeutic results cannot definitely be ascribed to the influence on the hypophysis or the ovary, since the endometrial pattern which reflects hypophysial gonadal relationship was frequently maintained in the status it had attained before implantation. Excessive bleeding was arrested in spite of the persistence, for instance, of the cystic glandular hyperplasia.

Since morphologic regression in the endometrium in general was not attained the therapeutic effect of testosterone propionate may be achieved through its inhibitory action on the vascular and muscular factors involved in menstruation.[5] Because of the observation that uterine fibroids decreased somewhat in size, a myotrophic property perhaps may be attributed to testosterone propionate. In this respect it is of interest to recall the work of Lipschütz and Vargas,[14a] who were able to offset the fibromatogenic effect of estrogens in the guinea pig by androgens. Abarbanel[15] attributed the therapeutic effect of testosterone propionate in menorrhagia to the sum total of the twofold effects of testosterone propionate, i. e. inhibition of intermittent uterine contractions and direct stimulation (constricting) action on myometrial elements.

The relative though temporary effectiveness of implanted testosterone proprionate pellets in menopausal patients is difficult to explain. The action cannot be due to inhibition of the pituitary activity, since in women with a normal cycle the rhythm was not disturbed even with doses up to 400 mg. The action may be due to estromimetic properties of testosterone propionate. Salmon[5] has attributed such properties to testosterone propionate when used in sufficient dosage, since castrate vaginal smears were converted to normal. This was confirmed by our studies. It was found that testosterone propionate in 400 mg. doses satisfactorily relieved the menopausal syndrome and in 2 patients prevented atrophic changes of the vaginal mucosa. However, when smaller doses were used the therapeutic effectiveness was less and of shorter duration and did not suppress vaginal maturation or prevent vaginal atrophy. Silberman and his associates[16] found

10. Loeser, A. A.: Subcutaneous Implantation of Female and Male Hormone in Tablet Form, Brit. M. J. **1**: 479 (March 23) 1940.
11. Geist, S. H.: Androgen Therapy in Gynecology, J. Clin. Endocrinol. **1**: 154 (Feb.) 1941.
12. Abarbanel, A. R.: Therapeutic Rationale for the Use of Testosterone Propionate in the Immediate Treatment of Functional Uterine Bleeding, Tr. Am. A. Obst. & Gynec. **52**: 163, 1939.
13. Geschickter, C. F.: Personal communication to the author.
14. Hartman, C. G.: The Effect of Testosterone on the Monkey Uterus and the Administration of Steroidal Hormones in the Form of Deansley-Parkes Pellets, Endocrinology **26**: 449 (March) 1940.
14a. Lipschütz, Alexander, and Vargas, Luis, Jr.: Prevention of Experimental Uterine and Extrauterine Fibroids by Testosterone and Progesterone, Endocrinology **28**: 669 (April) 1941.
15. Abarbanel, A. R.: Rationale for the Use of Testosterone Propionate in the Immediate Treatment of Excessive Uterine Bleeding, Am. J. Obst. & Gynec. **39**: 243 (Feb.) 1940.
16. Silberman, D.; Radman, H. M., and Abarbanel, A. R.: The Use of Testosterone Propionate in the Treatment of the Menopausal Patient, Am. J. Obst. & Gynec. **39**: 332 (Feb.) 1940.

that the subcutaneous implantation of pellets of testosterone propionate in doses of 25 mg. was the most satisfactory method of treating the menopausal patient.

In dysmenorrhea the action of testosterone propionate by pellet implantation can be only speculative at this time. The action, when therapeutically effective, may be due to a modification of uterine contractions. Both Robson [17] and Leonard [18] have shown that testosterone propionate suppresses uterine contractions in the rabbit. The anesthetic properties of certain steroids such as testosterone propionate have been stressed recently by Selye [19] and may account for some of the results obtained in dysmenorrhea, menorrhagia, pelvic discomfort and mastalgia.

The alleviation of the syndrome of nocturnal frequency in these patients was due to some specific action of the implanted steroid and cannot be attributed to the minor decrease in size of the tumors which frequently occurred.[20] There are many indications that the genitourinary tract is under hormonal influence. This may be adduced from the following facts: 1. One of the first symptoms associated with early pregnancy is a disorder of micturition. 2. In pregnancy, hypertrophy and dilatation of the ureters and other genitourinary disturbances may occur. 3. In the climacteric, urinary frequency, urgency and incontinence are common accompaniments of the menopausal syndrome. Mocquot and Moricard [21] were the first to employ compounds of testosterone for the alleviation of disorders of micturition in menopausal patients. Recently, Salmon and his associates [22] were able to keep menopausal patients with disorders of micturition symptom free by large doses of estrogenic hormone. These patients appeared refractory to orthodox treatment. 4. Experimental data prove that certain components of the genitourinary tract are under hormonal influence. Castration of the male rat is followed by a decrease in weight of the kidneys. This reduction in weight can be prevented by the administration of chemically pure androgenic substances. Selye [23] believed that testosterone exerts a specific action on kidney tubules. Korenchevsky [24] has claimed that androgens are nephrotrophic, causing an increase in the weight of kidneys and in the size of tubules in both normal and castrate female rats.

Libido is a highly complex function in which psychologic, anatomic, neurologic, sentimental and hormonal components play important roles. The role of the hormonal component has not received due attention.[25] The increase in libido in the female following the administration of chemically pure androgenic substance in one form or another must be the result of a specific pharmacologic effect. Libido may be spoken of as a phenomenon depending on well defined chemical substances. The action may be mediated through minor changes in electrolyte balance or the effect may be directly on specific organs. In some patients frigidity was due to dyspareunia because of dryness of the vagina. Following testosterone propionate pellet implantation libido returned and increased mucinification of the vaginal epithelium was noted with resultant improvement in sexual relations. Hartman [14] noted that the action of testosterone on the sex skin of the female monkey invariably was estrogenic. The sex skin was always brilliant red.

17. Robson, J. M.: Reactions of Uternie Muscle and Endometrium in Rabbits to Testosterone, Quart. J. Exper. Physiol. **26:** 355 (May) 1937.

18. Leonard, S. L.; Sager, V., and Hamilton, J. B.: The Effect of Male Hormone on Uterine Motility and the Uterus, Proc. Soc. Exper. Biol. & Med. **37:** 362 (Nov.) 1937.

19. Selye, Hans: Correlations Between the Chemical Structure and the Pharmacological Actions of the Steroids, Endocrinology **30:** 437 (March) 1942.

20. Greenblatt, R. B.: A New Syndrome of Nocturnal Frequency Due to Endocrine Imbalance, J. M. A. Georgia, to be published; Syndrome of Nocturnal Frequency Alleviated by Testosterone Propionate, J. Clin. Endocrinol. **2:** 321 (May) 1942.

21. Mocquot, P., and Moricard, R.: Etude préliminaire des effects provoques par l'hormone male sur les troubles functionnels urinaires de femme et de l'utilisation males en gynecologie, Bull. Soc. d'obst. et de gynéc. **25:** 787 (Dec.) 1936.

22. Salmon, U. J.; Walter, R. I., and Geist, S. H.: The Use of Estrogens in the Treatment of Dysuria and Incontinence in Postmenopausal Women, Am. J. Obst. & Gynec. **42:** 845 (Nov.) 1941.

23. Selye, Hans: On the Protective Action of Testosterone Against the Kidney Damaging Effect of Sublimate, J. Pharmacol. & Exper. Therap. **68:** 454 (April) 1940.

24. Korenchevsky, V., and Ross, M. A.: Kidneys and Sex Hormones, Brit. M. J. **1:** 645 (April 20) 1940.

25. Greenblatt, R. B.; Mortara, F., and Torpin, R.: Sexual Libido in the Female, Am. J. Obst. & Gynec., to be published.

CONCLUSION

It appears that the pellet method of implantation has more nearly approached the endogenous mechanism of hormone secretion in the normal female organism. It is entirely rational to suppose that the exogenous administration of male hormone in this manner adequately and satisfactorily restored the normal ratio of androgenic and gynecogenic hormones. Clinical manifestations of disruption of this ratio were corrected without the untoward effects observed after administration of unphysiologic doses of androgenic substances by parenteral means.

ABSTRACT OF DISCUSSION

DR. WILLARD M. ALLEN, St. Louis: Excessive bleeding which occurs from the uterus during the menstrual period in some women with a myomatous uterus or in patients with functional bleeding has been variously explained, but any explanation must consider the condition of the blood vessels. The reduction of bleeding which Dr. Greenblatt has observed following the use of testosterone propionate must therefore be explained by some effect on the uterine vessels. One of the outstanding effects of estrogens is increased cyanosis and congestion of the uterus. Androgens are known to inhibit many of the effects of estrogens. I assume, therefore, that the reduction of bleeding was brought about by inhibition of the effect of estrogens on the vessels of the uterus. This is in accord with Dr. Greenblatt's observation that myomas have decreased in size while the patient is under the influence of testosterone. The question which arises is whether this effect is a direct inhibitory action of the normal effect of estrogen or whether the supposed change is due to an actual diminution in the amount of estrogen produced by the ovary. Testosterone does affect the anterior lobe of the pituitary and thus indirectly leads to ovarian atrophy. This is not likely to be the explanation of his results, since many of his patients had essentially normal cycles afterward. We all know that when the ovary is unduly inhibited the menstrual cycle is liable to be affected. Dr. Greenblatt has observed, I believe, that most of the patients getting testosterone had a considerable increase in libido. I think we are inclined to believe that estrogen is responsible for such sexual desire in the female, and, conversely, that androgen is the motivating agent in the male. This is not entirely correct. In some mammals progesterone is a much better agent for the induction of sexual receptivity than is estrogen. Mating, for instance, can be induced with regularity in castrated female rats and guinea pigs which have been primed with estrogen by a single injection of progesterone. The increased libido in these women under the influence of androgen may, in fact, be directly due to changes in the clitoris and the vulvar region brought about by the use of testosterone. We know that if large doses of testosterone are given there is hypertrophy of the clitoris.

DR. UDALL J. SALMON, New York: Androgen therapy has been a major interest of mine for the last six years. As regards the value of androgen therapy in gynecology, there is a divergence of opinion. The group with which I am associated at the

Mount Sinai Hospital feels that androgen therapy has a sound rationale based on experimental studies in women and supported by a wide clinical experience. Last year, before this section in Cleveland, Dr. Geist and I presented our experience with androgen therapy in a variety of gynecologic disorders. The series of cases totaled over 400, the period of observation varying from six months to more than four years. That series included a group of 40 cases in which testosterone and testosterone propionate were implanted both in the form of loose crystals and in the form of pellets, varying in dosage from 50 mg. to 675 mg. Our studies revealed that, if one administers more than 500 mg. of testosterone propionate to women during the course of one cycle, certain striking biologic effects result. The hypophysis is inhibited; ovulation fails to occur; estrogen and progesterone formation is suppressed, and, as a result of that, involutional (estrogen deficiency) changes occur in the endometrium and in the vagina. The threshold for these effects is about 500 mg. It is also, incidentally, the threshold for the induction of the virilization symptoms. Fortunately the hormone is clinically effective in much smaller doses, so that it is possible to exploit the therapeutic properties of this hormone in the female without risking the danger of inducing any of these virilization phenomena. One aspect of androgen therapy that Dr. Greenblatt did not have time to elaborate was the effect of androgen on libido. Dr. Geist and I have completed a study on the effects of testosterone propionate on the sexual reactions of women. Our observations led to the following conclusions: Androgens (*a*) cause a heightened susceptibility to psychic and somatic sexual stimulation, (*b*) produce an increased sensitivity of the external genitalia and (*c*) induce a greater intensity of sexual gratification. This property of the androgens is, however, not an unadulterated virtue, since if administered in excess to women with normal libido it may cause abnormal intensification of desire and may lead to marital complications. Our experience with the implantation of androgens has not been as satisfactory as Dr. Greenblatt's. In a few instances, chiefly cases of premenopausal menometrorrhagia, we have had good therapeutic results, but in the majority the implantations were either ineffective or produced hypertrichosis or acne, necessitating excision of the pellets. Administration of androgens by implanations, we feel, unnecessarily complicates the procedure of androgen therapy without offering any advantages over the intramuscular or oral methods.

DR. L. F. HAWKINSON, Oakland, Calif.: In 1935 I pointed out that the menopausal syndrome was usually much more severe in patients who had hysterectomy or intrauterine radium. These patients often require five times the dose of estrogen to control the symptoms. The uterus probably plays a very important role in the maintenance of ovarian function. Although I have used few testosterone pellets in the female, in those patients in whom pellets were used the results were very satisfactory. For the past four years I have used testosterone propionate by hypodermic injection in the female and have never seen any virilism or effects that might be considered harmful. I have adopted a regimen in menopausal women who have menometrorrhagia, particularly those who have a tendency to bleed profusely when given estrogens. This regimen alternates estrogens with androgens. Two thousand rat units or 10,000 international units is given for two or three doses and then a dose of 10 or 25 mg. of testosterone propionate. The ratio between the estrogens and androgen is balanced so that the bleeding is controlled. The frequency of the dose of androgen is increased if the bleeding persists. In regard to libido, I find that the majority of patients who receive sufficient amounts of testosterone notice an increase in libido. The alleviation of menopausal symptoms by androgen alone requires large doses. A combination of estrogen and androgen relieves both the symptoms and excessive bleeding.

DR. CHARLES F. GESCHICKTER, Baltimore: I have been using pellet implantation for cancer cases for some years and have had a similar experience to that of Dr. Greenblatt. I have never given more than 100 mg. in the form of a pellet. Most of these patients receiving 20 mg. pellets have been treated at intervals of one to two months for periods as long as three years. I have never had any effects of virilism in these patients. The use of pellets is condemned by some. On scientific grounds I believe that it is certainly worth while in order to learn what is the role in therapy of the androgens, because experience in the laboratory teaches us that the hormone is about three times as efficient in the form of a pellet as it is by injection. Therefore, if we are to explore the field of androgen therapy, pellets properly used offer the hormone the most efficient chance to demonstrate what it can do. There are some words of caution, I think, that should be expressed when one discusses pellet therapy. I do not approve of the large pellets, which are more often extruded and, if not, will enable both the physician and the patient to take a three hundred day holiday. Particularly when one is treating myomas of the uterus or menorrhagia one must remember that bleeding from the uterus is a symptom of a great many conditions, and to mask it successfully with a form of pellet therapy and then to have that therapy last over a period of months is not without its danger. If one uses the smaller pellets one practically never gets extrusion. I do not have to use sutures, I never go down to the fascia, I do not have to use the operating room. A small wheal of procaine hydrochloride is used. I have never used more than 2.5 cc. of procaine. I use the bistoury scalpel and the mosquito forceps to spread. I try not to make the incision quite large enough; I make it small enough so that it has to be spread with the clamp in order to get the pellet in. I never put in a suture but seal with a strip of flamed adhesive plaster. Using that technic I have never had an extrusion or an infection. I think the pellet therapy could be made extremely simple, and it certainly is the efficient way to find out what the hormone can do.

DR. CARLOS A. P. LAMAR, Miami, Fla.: I have used implantation of pellets of pure testosterone instead of testosterone propionate, with results that parallel those of Dr. Greenblatt. The definite role of androgen in the treatment of excessive menstrual bleeding has been amply demonstrated. The implantation of pellets can be done without operative procedure, as the previous discusser has said. That is the routine that I ordinarily use. I have been observing the effect on libido for some time. I have noticed that the increase in libido is much more pronounced in women near the menopausal age than in younger women. Some women in the early twenties have been treated with parenteral doses of testosterone propionate as high as 1,200 mg. in one month without producing any symptoms of virilism and without increasing the libido. I have 2 of those cases at present.

DR. ROBERT B. GREENBLATT, Augusta, Ga.: I should like to say another word about libido, since limitation of time did not afford the opportunity to say much in my paper. Libido is a complex phenomenon depending on physiologic, sentimental and anatomic factors. We have neglected the hormonal aspects. In fact, it might be said that love, marital harmony and libido are influenced by blood chemistry. One might be bold enough to suggest that libido is purely a chemical test tube equation, but that would be going too far. Certainly libido may be increased in patients who have little or no libido and particularly in patients who once knew libido but have lost it. In this respect testosterone propionate probably has a specific pharmacologic action. In general I found that after pellet implantation the clitoris was not very much enlarged. However, when androgens were administered parenterally I found that enlargement of the clitoris was much more frequent. The amount of testosterone propionate that is made available to the organism by implantation of a 100 mg. pellet is small, for I found the average absorption that takes place over a period of eight months' time is only 0.3 mg. a day—a comparatively small amount. Masculinizing effects were not observed in any of the patients. Limitation of time prevents me from discussing the problems raised by the various speakers who were kind enough to discuss my paper. However, I agree with Dr. Geschickter that the technic can be improved. I recommend the method presented when large dosages are to be employed; but when small amounts of hormones are to be administered I see no objection to using his method of subcutaneous implantation.

THE EVALUATION OF ANTISEPTICS

ALBERT C. HUNTER, PH.D.
WASHINGTON, D. C.

The discovery or development of the "ideal" antiseptic is an objective much sought by research workers in the fields of bacteriology, chemotherapeutics and preventive medicine. Although this objective obviously has not yet been attained, it is apparent that diligent search continues for a chemical compound which has the characteristics of an ideal antiseptic, namely high germicidal or inhibitory properties, no tissue toxicity or at most a very low toxicity, freedom from specificity, efficiency in the presence of organic matter, power to penetrate, stability and perhaps other characteristics, including low cost. Efforts to produce useful, if not ideal, antiseptics have resulted in offering to the medical profession and to the public a wide variety of chemical substances, including mercurials, phenolic compounds, silver preparations, products of the liquor antisepticus type, dyes, halogen compounds and many others with staggering organic chemical designations. Most of these preparations are offered for general antiseptic purposes, although in some cases there is recognition among the informed, but not always disclosed on the label, that the compounds are relatively specific in their action on certain bacterial groups. Some preparations claim to be, and are, efficient germicides; others make no claim beyond the power to inhibit bacterial growth. A few preparations are offered for the "sterilization" of surgical and dental instruments. Substances proposed for the prevention and cure of certain mycotic infections are not uncommon.

The task of appraising the merits and demerits of such a group of substances with diverse properties becomes one of increasing magnitude and one possessing grievous obstacles to satisfactory evaluations by both the laboratory worker and the clinician. A review of the literature reveals a tendency to attempt to develop one universally applicable in vitro test, standardized in all of its details and yet with all its niceties, set up under conditions not in any way resembling those under which the antiseptic is expected to function in actual practice. In contrast to the investigator who chooses to evaluate solely on the basis of the laboratory test is the person who scorns in vitro procedures in their entirety and sees merit only in clinical results. Appraisals arrived at completely from clinical practice may too often be based on the acceptance of empirical observations as valid evidence of antiseptic efficacy without due consideration to all the uncontrolled factors.

United States Department of Agriculture circular 198 [1] has often been cited as the source of a "standard" or "official" method favorable response to which classes a substance as efficacious for the purpose recommended and consequently demonstrates its compliance with the requirements of the law. To the extent that the circular described procedures as those adopted by the Food and Drug Administration and suggested tests that could be applied to specific types of preparations, some justification has probably existed for such an opinion. However, this was not the intent of the document and is not a proper interpretation of its contents. Much has been written [2] to point out the fallacy of applying phenol coefficients to antiseptics as differentiated from disinfectants directly comparable with phenol. The so-called F. D. A. test utilizing Staphylococcus aureus as the test organism at its best provides information concerning the ability of the compound tested to destroy staphylococci only under the conditions of the test. Furthermore, Brewer [3] has called attention to the faulty interpretations which may follow too great dependence on Staph. aureus as a test organism for all types of preparations, some of which may be intended for the destruction of organisms of entirely different resistance. The F. D. A. test, the agar-plate tests and the wet filter-paper and dry filter-paper tests described in circular 198, within their limitations, serve a useful purpose. However, rather than to accept the results of any of these procedures as a sufficient measure of efficacy a more logical approach to the job of appraisal appears to lie in a broader concept of evaluation, which because of its difficulties of application has not been universally adopted, even though its principles have from time to time been outlined by those who specialize in this field.[4] To quote Browning: "Antiseptics intended for therapeutic use must not be considered *en bloc* or selected solely on the basis of their ability to kill rapidly some test organism in vitro. Each must be examined as regards selective action on various bacteria in protein as well as watery media in vitro, and as regards effects on tissues in vivo. Such tests give valuable indications, but the chemotherapeutic efficacy of a substance is finally determined by its influence on the pathogenic action of organisms in an infected host." This point of view, entirely sound in its expression, admits the impracticability of reaching a conclusion as to true efficacy from the results of a single in vitro test. The problem then becomes one of fitting together the results of old established procedures with clinical observations and with the results of additional tests, some recently developed and some not yet conceived, to form a complete picture of the properties of a substance under scrutiny.

In determining whether or not a product represented as an antiseptic meets the requirements of the Federal Food, Drug and Cosmetic Act of 1938 [5] the question of efficacy under conditions of use becomes a matter of paramount importance. All articles intended for use in the diagnosis, cure, mitigation, treatment or prevention of disease in man or other animals are classed as drugs within the meaning of that act and if shipped or offered for shipment in interstate commerce must comply with the provisions of the statute. Section 201(*o*) of the act states: "The representation of a drug, in its labeling, as an antiseptic shall be considered to be a representation that it is a germicide, except in the case of a drug purporting to be, or represented as, an antiseptic for inhibitory use as a wet dressing, ointment, dusting powder, or such other use as involves prolonged contact with the body." It is then pertinent to give heed to the requirement of 502(*f*), which defines a drug as misbranded unless its labeling bears adequate directions for use. Furthermore, 201(*n*) of the law provides that

From the United States Food and Drug Administration.

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1. Ruehle, G. L. A., and Brewer, C. M.: United States Food and Drug Administration Methods of Testing Antiseptics and Disinfectants, Circular 198, United States Department of Agriculture, 1931.

2. Reddish, G. F.: Limitations of the Phenol Coefficient, Indust. & Engin. Chem. **29**: 1044-1047, 1937. Ruehle and Brewer.[1]

3. Brewer, C. M.: Use and Abuse of Staphylococcus Aureus as a Test Organism, Am. J. Pub. Health **32**: 401-405 (April) 1942.

4. Browning, C. H.: The Value of Antiseptics in the Control of Bacterial Infections, Brit. M. J. **2**: 579 (Sept. 29) 1934. Reddish, G. F.: Recent Developments in Methods of Testing Germicides, Indust. & Engin. Chem. (Analyt. Edition) **10**: 425 (Aug. 15) 1938.

5. Federal Food, Drug, and Cosmetic Act and General Regulations for Its Enforcement. Federal Security Agency Service and Regulatory Announcements, F. D. C. 1, August 1939; revised, August 1941.

"in determining whether the labeling is misleading there shall be taken into account (among other things) not only representations made or suggested . . . but also the extent to which the labeling fails to reveal facts material in the light of such representations. . . ." A self-imposed standard of performance is thus set up for each product by its labeling claims. Failure to function in conformity with those claims renders a product adulterated or misbranded within the meaning of the act.

In evaluating the efficacy of preparations in the light of these legal requirements the single in vitro test may be applicable to one class of products, namely those which fail to exhibit any inherent germicidal or bacteriostatic properties even under the most favorable laboratory conditions. Obviously they are without value and need not be tested further.

Dissatisfaction with the old procedures is apparent from the contributions to the bacteriologic and medical literature made in the past decade, proposing methods designed to provide information to facilitate evaluation of antiseptics under conditions of use. Browning,[4] Hunt,[6] Kempf and Nungester[7] and Sarber,[8] among others, have proposed in vivo methods. In some of the proposed methods lesions on laboratory animals are produced and treated in situ, while in others the animal is used as a culturing medium to test the pathogenicity of the test organisms surviving treatment with the antiseptic on or within the infected host. The method of Price[9] involving the examination of skin washings following treatment has received attention. Animal tests of the type proposed have been generally subject to criticism based on the variability of the individual and on the lack of control possible over all elements of the test. Regardless of the validity of the criticisms in specific cases, merit must be ascribed to any reasonable in vivo procedure on the theory that such tests provide some information concerning performance of an antiseptic in the presence of living tissue and contribute some evidence to supplement that obtained by other procedures.

Notable among the advances made in this field are those methods designed to determine the toxic effect of antiseptics on tissue as contrasted with their effect as germicides. While essentially in vitro tests, these methods depart radically from the strictly cultural procedures and provide valuable data to throw light on reactions that may be expected under conditions of body use. In 1935 Salle and Lazarus[10] proposed a method of evaluation based on a comparison of the resistance of bacteria and embryonic chick heart tissue to germicidal substances. By dividing the highest dilution of an antiseptic required to prevent growth of embryonic tissue embedded in plasma diluted with Tyrode's solution by the highest dilution required to kill the test organism, Salle and his associates[11] computed toxicity indexes for a number of well known substances used as antiseptics. From their tests they concluded that in general the simple inorganic substances rated higher than the newer and more complex compounds. The factor of tissue toxicity in the evaluation of antiseptics was also discussed by Nye,[12] who gave consideration to the harmful effects of antiseptics on white blood corpuscles. In reports[13] dealing with the toxicity of antiseptics, Welch and his associates, after describing a method for determining the effect of chemical antisepsis on phagocytosis, explained the mechanism of the toxic action of germicides on whole blood by stating that impairment of the phagocytic function of the leukocytes is a primary effect exerted by the antiseptic against the humoral, in contrast to the cellular, elements of the blood. In pursuing toxicity tests based on determination of the loss of activity or actual destruction of the leukocyte, recognition is granted to the part normally played by such cells in protection against invading organisms. It is reasonable to conclude that a substance used as an antiseptic should augment rather than interfere with the activity of these cells and that any compound strikingly more toxic for leukocytes than for bacteria should thereby acquire demerits as an antiseptic. Applying the toxicity test using whole blood as a tissue, Welch, with others, reported the toxicity indexes of a number of antiseptic substances, including preparations containing soap and alcohol, particular attention being directed to mouthwashes.[14] Of eighty-seven mouthwashes tested, sixty-two in 1:5 dilution exerted a toxic effect on blood as measured by impairment of phagocytosis; the remainder were toxic in higher dilutions. By comparison with their power to function as germicides in the presence of whole blood, toxicity indexes greater than 2 were determined in every instance. The authors of the report referred to frankly recognize the impossibility of evaluating antiseptics for all their uses by application of the toxicity test alone. On the other hand, they do point out the value of data derived from that test in supplementing other data to arrive at a proper appraisal of an antiseptic.

Bronfenbrenner, Hershey and Doubly[15] also utilize tissue in a procedure proposed as helpful in the evaluation of germicides. By their method the concentration of disinfectant necessary to cause 50 per cent reduction in the rate of oxygen uptake by mouse liver cells in saline suspension is determined and is compared with the concentration causing 50 per cent inhibition of the rate of oxygen consumption by a suspension of Escherichia coli. The authors report that data for tissue toxicity obtained with several disinfectants are in satisfactory agreement with values obtained by intraperitoneal injection into the mouse.

Perhaps in some of their aspects the newer tests do not lend themselves to the rigid "standardization" of

6. Hunt, G. A.: The Use of Cutaneous Staphylococcus Lesions in Mice for the Evaluation of the Germicidal Activity of Disinfectants, J. Infect. Dis. **60**: 232-237 (March-April) 1937.

7. Kempf, A. H., and Nungester, W. J.: An In Vivo Test for the Evaluation of Skin Disinfectants, J. Bact. **43**: 49-50 (Jan.) 1942.

8. Sarber, R. W.: An In Vivo Method for the Evaluation of Germicidal Substances Used for Skin Disinfection, J. Bact. **43**: 50 (Jan.) 1942.

9. Price, P. B.: The Bacteriology of Normal Skin: A New Quantitative Test Applied to a Study of the Bacterial Flora and the Disinfectant Action of Mechanical Cleansing, J. Infect. Dis. **63**: 301-318 (Nov.-Dec.) 1938.

10. Salle, A. J., and Lazarus, A. S.: A Comparison of Resistance of Bacteria and Embryonic Tissue to Germicidal Substances, Proc. Soc. Exper. Biol. & Med. **32**: 665-667 (June) 1935.

11. Salle, A. J.; McOmie, W. A., and Shechmeister, I. L.: A New Method for the Evaluation of Germicidal Substances, J. Bact. **34**: 267-273 (Sept.) 1937. Salle, A. J.; McOmie, W. A.; Shechmeister, I. L., and Foord, D. C.: The Evaluation of a Group of Germicides by the Tissue Culture Technic, ibid. **37**: 639-646 (June) 1939.

12. Nye, R. N.: The Relative In Vitro Activity of Certain Antiseptics in Aqueous Solution, J. A. M. A. **108**: 280-287 (Jan. 23) 1937.

13. Welch, Henry, and Hunter, A. C.: A Method for Determining the Effect of Chemical Antisepsis on Phagocytosis, Am. J. Pub. Health **30**: 129-137 (Feb.) 1940. Welch, Henry: Mechanism of the Toxic Action of Germicides on Whole Blood Measured by the Loss of Phagocytic Activity of Leukocytes, J. Immunol. **37**: 525-533 (Dec.) 1939. Welch, Henry; Brewer, C. M., and Hunter, A. C.: Toxicity of Antiseptics; Experiments with Hemolytic Complement, ibid. **38**: 273-282 (April) 1940.

14. Welch, Henry and Brewer, C. M.: Relative Toxicity of Certain Antiseptics Containing Soap and Alcohol, with Special Reference to Mouthwashes, Am. J. Pub. Health **32**: 261-267 (March) 1942. Welch, Henry, and Brewer, C. M.: The Toxicity Indexes of Some Basic Antiseptic Substances, J. Immunol. **43**: 25-30 (Jan.) 1942. Welch, Henry; Slocum, G. G., and Hunter, A. C.: Method for Determining the Toxicity of Antiseptics as Measured by the Destruction of Human Leukocytes, J. Lab. & Clin. Med. **27**: 1432-1438 (Aug.) 1942.

15. Bronfenbrenner, J.; Hershey, A. D., and Doubly, J.: Evaluation of Germicides by a Manometric Method, J. Bact. **37**: 583-597 (June) 1939.

the phenol coefficient procedure. However, it is not unreasonable to permit some relaxation on that point. In actual practice the user of antiseptics is not confronted with standard subjects for treatment nor is the infectious agent to be combated a standard factor. It may be suggested that in searching to learn the true merits of an antiseptic under conditions of use some of the niceties of standardized procedure might profitably be sacrificed.

Between the laboratory test and the results to be obtained in practice exists a gap which should be bridged by clinical observations and practical experience. If the laboratory studies are to be useful to the practitioner, they must be interpretable in terms of actual use. It is pertinent to point out the fallacy, for instance, of accepting as evidence of their efficacy as sterilizers of surgical and dental instruments chemical preparations which have been tested in the laboratory only against vegetative forms of bacteria. Reviews of that subject by Knighton [16] and Brewer [17] have thoroughly discussed the ineligibility of preparations to the designation of "sterilizer" until it has been proved that they are efficacious in the destruction of resistant bacterial spores. With respect to antiseptics for use on the body, if the laboratory tests for their evaluation do not take into consideration tissue toxicity and the interfering factors present in the living host, and not in the test tube, the conclusions drawn may be quite misleading. Speaking for the government agency charged with the enforcement of the Food, Drug and Cosmetic Act, there is no single "standard" or "official" test for the evaluation of antiseptics. The objective in testing a preparation claimed to be an antiseptic with prescribed directions for use is the collection of related parts of a picture to show not only the inherent germicidal or inhibitory properties of the compound but the degree of efficacy with which these properties are applied under the conditions of use.

ABSTRACT OF DISCUSSION

DR. WARD J. MACNEAL, New York: In evaluating antiseptic and germicidal agents a distinction should be drawn between three groups of these agents: (1) those acting at a distance from the human host, (2) those acting on epithelial surfaces or on superficial wounds and (3) those designed to act after absorption into the circulating fluids. These may be designated respectively as (1) disinfectants, (2) antiseptics in the narrower sense and (3) anti-infectious therapeutic agents, chemical and biologic. There is no single easy and simple method of evaluating all these agents. For those acting at a distance the harmful property may be wholly vitiated before reaching the host. An agent to be used for quick action on a body surface should be effective against the germs and should not be dangerously toxic in the amounts absorbed. Local tissue toxicity, which has been featured by Fleming and also by Welch and Hunter in previous papers, seems to have been too greatly stressed by these authors. As Professor Garrod has said, the local destruction of tissue is a small price to pay in consideration of the control of the infectious agent. Remote toxicity after absorption is of greater moment, as for example in the nervous system after alcohol or sulfamethylthiazole, in the myocardium after sulfonamides in general, in the liver after arsenicals, in the kidneys after mercurials. Direct experimental tests on animals would seem most logical. Such tests present difficulties, and not all microbes are adapted to such examination. All kinds of in vitro tests should be welcomed. We need to be on guard against accepting a tricky result obtained by some special procedure designed to extol or to condemn some particular agent. By omitting the well known step of inactivation, one may exaggerate the apparent germicidal action of iodine, and by testing alcohol or liquor antisepticus in too dilute form one may easily cast discredit on their germicidal value. Errors of this sort were current thirty years ago but should hardly be expected at present. Infectious agents are many in nature, and one drug may not be effective against all. It has recently been shown that viruses of vaccinia and influenza are quickly inactivated by liquor antisepticus although relatively resistant to some other antiseptics. I would plead, therefore, for a broadminded approach which welcomes all obtainable information about the properties of any antimicrobic agent.

DR. ALBERT C. HUNTER, Washington, D. C.: The first class of products that Dr. MacNeal mentioned is classified as disinfectants, since they are to be used on inanimate objects. I did not mean to include them in the paper at all. In our work we have an arbitrary division, because disinfectants for use on inanimate objects are subject to control by another law. When one says antiseptics one is thinking of drugs for use in or on the body. I agree with the statements Dr. MacNeal made about not applying the toxicity test to disinfectants. Furthermore, the toxicity test on antiseptics is not used as a universal test to the exclusion of all others. My point is that there is no universal test. What we propose to do is like the assembling of the pieces of a jigsaw puzzle. We determine the inherent killing and inhibitory powers in test tube culture and the tissue toxicity and obtain other pertinent data. If we put the pieces together and they make a good picture the product has merit accordingly. If it is a bad picture that is what we want to find out too. I should like to leave it clear that officially we are not presenting the toxicity test or any other single test as the sole measure of the efficacy of an antiseptic.

16. Knighton, H. T.: Significance of Tests for the Evaluation of Antiseptics and Germicides, J. Am. Dent. A. **26:** 2047-2055 (Dec.) 1939.
17. Brewer, J. H.: The Antibacterial Effects of the Organic Mercurial Compounds, J. A. M. A. **112:** 2009-2018 (May 20) 1939.

CIRCULATORY ADJUSTMENTS DURING HIGH SPINAL ANESTHESIA

E. M. PAPPER, M.D.
S. E. BRADLEY, M.D.
AND
E. A. ROVENSTINE, M.D.
NEW YORK

It is generally agreed among experienced surgeons and anesthetists that hypotension is a corollary of high spinal anesthesia. However, any discussion of the cause, the significance to the patient's welfare or the optimum treatment for the fall in blood pressure so regularly observed while operation is in progress during high spinal anesthesia would provoke many arguments. Theoretical discourses, data from laboratory experiments and clinical investigations of spinal anesthesia have multiplied with the years since the method was first advocated, and no small fraction of this accumulated literature is devoted to the problems concerned with the circulatory adjustments. Despite these efforts, the problems await solution and, notwithstanding the fact that a decided fall in blood pressure from whatever cause must be considered unphysiologic, this complication during spinal anesthesia has not been evaluated satisfactorily in terms of morbidity and mortality.

It is important to evaluate accurately the effects of spinal anesthesia on the circulation, since the procedure has such a prominent role in present day abdominal surgery. The flaccid relaxation of abdom-

Dr. Bradley is Commonwealth Fund Fellow.
From the departments of anesthesia, physiology and surgery, New York University College of Medicine.
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inal muscles and the strong intestinal contractions produced by spinal anesthesia have a fascinating and legitimate appeal to many surgeons. Moreover, with the methods available for anesthesia there is no agreement among anesthetists as to the relative merits of spinal and inhalation anesthesia in the anesthetic control of the abdomen. In this discussion, therefore, the laboratory and clinical data which have been prominently displayed to determine and explain the factors concerned in the circulatory adjustments to spinal anesthesia will be briefly but critically reviewed. Additional clinical data are presented also, and their significance in surgery during high spinal anesthesia is suggested.

Among the theories advanced, and in most instances supported, by laboratory investigations as the pathogenesis of the fall in blood pressure during spinal anesthesia are (1) hematogenous intoxication, (2) direct action on the medulla, (3) paralysis of adrenal nerves with reduced secretion of epinephrine, (4) the anoxia theory, (5) paralysis of the vasoconstrictor fibers in the anterior spinal roots and (6) the theory of stagnation in the postarteriolar bed.

HEMATOGENOUS INTOXICATION

It was proposed that the rapid absorption into the blood stream of anesthetic drugs injected subdurally might precipitate the hypotensive effects observed.[1] This was held untenable when it was conclusively demonstrated that intravenous injections of such drugs do not produce the severe or protracted disturbances in circulation that occur after intraspinal injection.[2] The theory is without support at the present time.

DIRECT ACTION ON THE MEDULLA

The theory of direct action on the medulla presupposed that the vital centers in the brain stem are more sensitive to the anesthetic agent than are the nerve roots emanating from the spinal cord. There is substantial evidence that such is not the case.[3]

PARALYSIS OF ADRENAL NERVES WITH REDUCED SECRETION OF EPINEPHRINE

Since the adrenal glands derive their innervation from the celiac plexus and the splanchnic nerves, paralysis of these nerves during high spinal anesthesia might be expected to reduce the supply of epinephrine to the body and thus produce a fall in blood pressure.[4] There are two objections to this thesis: First, Bazett [5] and Durant [6] point out that ligation of the adrenal veins or bilateral adrenalectomy is not accompanied by a fall in blood pressure. Second, Smith [7] maintains that the administration of epinephrine to man causes considerable arteriolar dilatation and produces, if anything, a fall in diastolic pressure and a well maintained or increased systolic pressure. It is difficult to understand, therefore, how absence of the adrenal hormone could produce vasodilatation if the converse is true. This theory no longer enjoys any degree of popularity.

1. Klapp, R., cited by Schuberth.[19]
2. Bower, J. O.; Clark, J. H.; Wagoner, G., and Burns, J. C.: Spinal Anesthesia, Surg., Gynec. & Obst. **54**: 882-897 (June) 1932.
3. Vehrs, G. R.: Spinal Anesthesia: Technics and Clinical Application, St. Louis, C. V. Mosby Company, 1934.
4. Perl, J. I.: Intra-Abdominal Use of Epinephrine in Hypotension During Spinal Anesthesia, Am. J. Surg. **17**: 275-278 (Aug.) 1932.
5. Bazett, H. C.: Time Relations of Blood Pressure Changes After Excision of Adrenal Glands, with Some Observations on Blood Volume Changes, J. Physiol. **53**: 320-338 (Feb.) 1920.
6. Durant, R. R.: The Blood Pressure of Adrenalectomized Rats, Am. J. Physiol. **85**: 364-365 (April) 1928.
7. Smith, H. W.; Rovenstine, E. A.; Goldring, W.; Chasis, H., and Ranges, H. A.: The Effects of Spinal Anesthesia on the Circulation in Normal, Unoperated Man with Reference to the Autonomy of the Arterioles, and Especially Those of the Renal Circulation, J. Clin. Investigation **18**: 319-341 (May) 1939.

THE ANOXIA THEORY

The anoxia theory as promulgated by Gray and Parsons [8] is based on observations on man and dogs that the blood pressure falls in proportion to the amount of intercostal muscle paralysis. Thus the circulatory changes are secondary to anoxia produced by decreased pulmonary ventilation. Seevers and Waters [9] supported this theory and demonstrated the return of blood pressure to normal or above normal by the administration of oxygen during artificial respiration in animals anesthetized to the fifth thoracic vertebra or above.

The thesis of anoxia as the cause of hypotension in spinal anesthesia is subject to criticism on several counts. The correction of hypotension in dogs under high spinal anesthesia may be accomplished by change in position, as shown by Burstein,[10] who noted the usual fall in blood pressure in the supine position in dogs whose subarachnoid space was continuously perfused with a 3 per cent solution of procaine hydrochloride and an immediate return to normal blood pressure by being placed in the right or left lateral position despite the maintenance of anesthesia to the cervical cord. It is thus quite probable that the fall in blood pressure noted in the experiments of Seevers and Waters may be due to the embarrassment of venous return by an increase of the aspiration of blood into the thorax during artificial respiration and passive massage of the vessels in the abdomen and chest. Since measurements of cardiac output were not made and artificial respiration without oxygen was not done, the interpretation of these data is open to question and might profitably lend itself to further study.

Further objection to the anoxic theory is made because of the use of anesthetized and premedicated animals. These objections will be elaborated on more fully in a consideration of the theory of arteriolar dilatation.

PARALYSIS OF THE VASOCONSTRICTOR FIBERS IN THE ANTERIOR SPINAL ROOTS

The theory of vasoconstrictor paralysis in spinal anesthesia producing hypotension by arteriolar dilatation has among its adherents most investigators of spinal anesthesia. It is supported by Babcock,[11] Burch and Harrison,[12] Ferguson and North [13] and many others. Because of the wide support of this thesis, which we do not accept, the evidence for the importance of tonic activity of the vasoconstrictor fibers in maintaining blood pressure must be examined critically.

The concept of vasotonic activity in the sympathetic nervous system in normal animals is based largely on the fact that the blood pressure falls or the peripheral blood flow increases immediately after surgical section of the splanchnic fibers in anesthetized cats and dogs. The major criticism of all this work and of the conclusions drawn is that observations were made in almost all instances on anesthetized animals.

8. Gray, H. T., and Parsons, L.: Blood Pressure Variations Associated with Lumbar Puncture, and the Induction of Spinal Anesthesia, Quart. J. Med. **5**: 339-367 (April) 1912.
9. Seevers, M. H., and Waters, R. M.: Respiratory and Circulatory Changes During Spinal Anesthesia, J. A. M. A. **99**: 961-968 (Sept.) 1932.
10. Burstein, C. L.: Postural Blood Pressure Changes During Spinal Anesthesia: A Preliminary Experimental Report, Anesth. & Analg. **18**: 132-139 (May-June) 1939.
11. Babcock, W. W.: Blood Pressure in Relation to Spinal Anesthesia, Anesth. & Analg. **4**: 222-228 (Aug.) 1925.
12. Burch, J. C., and Harrison, T. R.: The Effect of Spinal Anesthesia on Arterial Tone, Arch. Surg. **22**: 1040-1044 (June) 1931.
13. Ferguson, L. K., and North, J. P.: Observations of Experimental Spinal Anesthesia. Surg., Gynec. & Obst. **54**: 621-634 (April) 1932.

Knoefel[14] has shown evidence for widespread sympathetic excitation in man during ether anesthesia. As further evidence for sympathetic stimulation from ether and also urethane, the work of Elliott[15] may be cited in which the intact adrenal glands of anesthetized cats may be depleted of its content of epinephrine. Ether also causes constriction of the spleen.[16] In fact, so effective is the pressor action of ether that it has been used to elevate the blood pressure during spinal anesthesia.[11] However, ether has been shown also to have vasodilator effects.[17] Thus it is impossible to predict the net effect on observations pertinent to the circulation during spinal anesthesia in previously etherized animals.

Criticism of the use of morphinized animals in studies on spinal anesthesia is equally valid, since morphine promotes anoxia and hypercapnia by depressing the respiratory center. Although there is no evidence that anoxia and hypercapnia contribute to the hypotension observed during spinal anesthesia or sympathectomy, the possibility cannot be omitted that morphine also promotes muscle relaxation and may thus cause or aggravate venous stagnation. Seevers and Waters[18] admit that morphine, scopolamine, barbiturates and other anesthetic agents contribute to the hypotension observed during spinal anesthesia.

In view of these facts and the lack of attempt to evaluate the effects of laboratory and surgical manipulation in the experiments supporting the principle of vasoconstrictor paralysis as the cause of hypotension in spinal anesthesia, experimental work on anesthetized and traumatized animals cannot be accepted as valid support for this thesis.

THEORY OF STAGNATION IN THE POSTARTERIOLAR BED

If vasodilatation is the cause of the fall in blood pressure in spinal anesthesia, there should be an increased venous pressure and cardiac output, provided the reduction of blood pressure is moderate in degree. However, if venous stagnation is the cause, it should be accompanied by a decreased stroke volume and decreased cardiac output. Schuberth[19] reports cardiac output in 14 cases determined by Grollman's technic with anesthesia as high as the xiphoid or nipples. In 10 of these the cardiac output fell as compared with the control valve before anesthesia, and the blood pressure was noted to decrease in proportion. In the other 4 cases, the cardiac output increased with increased systolic pressure in 2, no change in 1 and a slight fall in 1. He also noted clinically that the veins were collapsed and interpreted this as evidence for decreased venous pressure. The arteriovenous oxygen difference was increased. These data led the author to conclude that the fall in cardiac output resulted in a decreased arterial pressure and that decreased cardiac output was due to an impaired return to the heart. This, in turn, was attributed to paralysis of the vasoconstrictor nerves. The difficulty of reconciling decreased venous pressure, decreased cardiac output and increased arteriovenous oxygen difference with arteriolar dilatation short of circulatory collapse is not explained. If the blood pressure changes are due to arteriolar dilatation, the reverse should be the case; that is, an increased cardiac output, increased venous pressure and decreased arteriovenous oxygen difference.

Other data supporting the notion of venous stagnation as the causative factor in the production of hypotension in man are available in the literature. Investigations of Burch and Harrison[20] and of Koster[21] and investigations presented here have demonstrated a fall in cardiac output of greater or less degree during spinal anesthesia. Schuberth[19] has shown an increased arteriovenous oxygen difference. The effects of high spinal anesthesia on venous pressure in man have been studied.[22] A fall in venous pressure of 25 per cent and a parallel fall in arterial pressure in anesthesia of the fourth thoracic vertebra or above was recorded. It was also pointed out that the venous pressure will fall in high spinal anesthesia irrespective of arterial pressure changes. As a corollary to venous stagnation, the circulation time should increase. An increase has been observed in man during high spinal anesthesia.[23] Finally, if arteriolar dilatation is not the important factor in the hypotension of spinal anesthesia, the diastolic blood pressure and the over-all peripheral resistance will be relatively unaffected. Smith and his associates[7] demonstrated remarkably little change in the diastolic blood pressure during high spinal anesthesia in man, and it has been pointed out that peripheral resistance decreased significantly in only 1 of 7 patients, decreased slightly in 2 others, was unchanged in 2 and increased in 2.[24] Thus the preponderance of evidence controverts the thesis of arteriolar vasodilatation as the cause of hypotension during high spinal anesthesia and supports the principle of postarteriolar bed stagnation as the most important factor. In this connection, in order to evaluate the response to spinal anesthesia seen in the operating room, it is interesting to point out the effects of high spinal anesthesia on the circulation in normal man under standard conditions not given premedication or operated on and to contrast the results with those seen during surgical manipulations.

Smith and his associates[7] studied 18 subjects in whom anesthesia reached at least as high as the fifth thoracic with motor paralysis to the lower extremities, abdomen and thorax. In 2 of these subjects the systolic and diastolic pressures were well maintained. The remaining subjects had some decrease in either the systolic or the diastolic pressure or both. However, the systolic pressure fell more than the diastolic and in all but 5 instances the diastolic did not fall below 60 mm. of mercury and frequently maintained its control level. The average fall in mean pressure was only 14 per cent in all cases. Since the heart rate was reduced only slightly, it was postulated

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that the fall in arterial pressure (which was not pronounced) was due to a fall in stroke volume occasioned by a decreased venous return because of pooling of blood in the paralyzed musculature. These observations were strengthened by studies [24] which showed that there was a reduction in cardiac output measured by the ballistocardiographic method in all of 7 instances. We observed relatively minor changes in heart rate and demonstrated that the reduction in cardiac output was due to a fall in stroke volume. We also observed an average fall in mean pressure of 14 per cent as measured by the Hamilton optical manometer after direct arterial cannulation, with anesthesia to the fifth thoracic or above.

The data cited were obtained in the presence of adequate denervation of the vasomotor fibers in the anterior spinal roots by spinal anesthesia. Information on this point was obtained by a comparison of the responses to postural change and the inhalation of low oxygen atmospheres and excess carbon dioxide in normal and anesthetized subjects. Hypercapnia in the normal subject produces an instantaneous and decided rise in systolic and diastolic pressure. This response was absent in spinal anesthesia to the fifth thoracic vertebra or above. Anoxemia likewise produces some hypertension in normal man but does not in high spinal anesthesia. Finally, the normal person responds to the upright posture with a well maintained blood pressure owing to vasoconstriction. The erect position, on the other hand, when high spinal anesthesia is given, causes a fall in blood pressure with the systolic falling faster than the diastolic, a bradycardia, vertigo and syncope. These effects are not instantaneous but occur gradually over one to three minutes. The evidence cited demonstrates the effectiveness of sympathetic denervation in high spinal anesthesia.

High Spinal Anesthesia in Two Hundred and Forty-Three Cases

Complications	Hypotension *			
	Severe, 30 per Cent	Moderate, 40 per Cent	Slight, 21 per Cent	None, 9 per Cent
During surgery (listed according to blood pressure changes)				
Nausea	13	15	14	17
Nausea and emesis	14	12	8	4
Syncope	6	1	0	0
Postoperative				
Nausea and emesis	5	3	0	0
Headache	2.5	4	0	9
Shock	4	1	0	0
Pneumonia	2.5	2	4	4
Death	5.5	5	4	0

* The index for hypotension used: a fall in mean pressure of 40 per cent plus is severe, 20 to 39 per cent moderate and 1 to 19 per cent slight.

CLINICAL STUDIES

To illustrate the contrast in hemodynamic activity of patients in the clinic with man not operated on, 243 consecutive clinical patients on whom operation had been performed during spinal anesthesia were analyzed in an entirely unselected manner. The only criterion was the requirement that anesthesia was at the sixth thoracic vertebra or above. Various drugs commonly used in spinal anesthesia, such as procaine hydrochloride, nupercaine, pontocaine hydrochloride, intracaine and monocaine, were employed. Most patients had previously been given small amounts of morphine and scopolamine and some had been given soluble pentobarbital also. A prophylactic injection of ephedrine sulfate was given intramuscularly to some patients before the anesthetic, and others received the drug to combat a fall in blood pressure during the course of the procedure. Various operations were performed but the majority were intra-abdominal manipulations. Criteria as to severity of blood pressure fall were arbitrarily selected. A fall in mean pressure of 40 per cent or more was considered severe, a reduction of 20 to 39 per cent moderately severe, and one of 1 to 19 per cent slight. In addition, there were patients who had no reduction or had a definite rise in blood pressure.

It is apparent from the accompanying table that 30 per cent of the patients had a severe fall in blood pressure and 21 per cent a slight fall and for 9 per cent no fall was recorded. A total of 70 per cent of patients exhibited significant hypotension. These findings contrast strongly with the effects of spinal anesthesia on the blood pressure of normal man in the supine position, not given premedication or operated on. Smith and his associates [7] and we [24] found no instance of severe fall in blood pressure as defined here and a moderately severe fall in mean pressure in only 25 per cent of the cases studied as compared with 40 per cent in the operative series. In round figures, almost three fourths of the clinical patients exhibit significant hypotension whereas less than one fourth of the subjects not operated on show such changes.

Another extremely significant fact is not shown in the table. The fall in blood pressure, regardless of the type of surgery performed, occurred after the beginning of surgical manipulations in practically all instances. The manipulation may be rapid change of position, abdominal incision, leaning against the patient's thorax, handling of viscera, hemorrhage or the use of abdominal packs. That surgery in its various aspects is an important factor in producing a fall in blood pressure in spinal anesthesia seems obvious. The patient whose sympathetic nervous system is extensively denervated by spinal anesthesia (sixth thoracic vertebra or above) is competent from the point of view of the circulation to handle his needs in the resting state in the supine position, but trauma of any sort concomitant with operative manipulation in the face of vasomotor paralysis and loss of vasomotor defense may precipitate a significant reduction in blood pressure and, if severe enough, complete circulatory collapse.

It is interesting to note the effect of major disturbances of the circulation and respiration preoperatively on the course of blood pressure changes when surgery is being done during spinal anesthesia. Preoperative pulmonary complications have no noticeable influence on the maintenance of blood pressure during spinal anesthesia. The effect of arteriosclerotic cardiovascular disease is uncertain, since it was present preoperatively in 13 per cent of cases showing no fall in blood pressure and had the same incidence in the group exhibiting severe falls in blood pressure as in any other group.

It is noteworthy that the incidence of nausea as a complication during high spinal anesthesia is unaffected by the extent of the fall of blood pressure, whereas the incidence of emesis decreases with decreasing falls in blood pressure. Another interesting fact is the occurrence of syncope in 6 per cent of the cases

showing severe falls in blood pressure, 1 per cent in the moderately severe group and in no cases in which blood pressure fell only slightly or not at all. The postoperative complications as listed are self explanatory. Emphasis should be placed on the absence of postoperative shock in the groups showing little or no change in blood pressure and the absence of mortality in the group exhibiting no fall in blood pressure.

The problem of treatment of the hypotension observed during spinal anesthesia is important. Treatment should be directed toward increasing venous return to the heart to maintain adequate cardiac output and increasing the oxygen tension of partially unsaturated arterial and venous blood. The administration of oxygen provides a means for satisfying the latter need. Clinically and experimentally, oxygen administration is of definite benefit in combating hypotension and the nausea and vomiting which may occur with spinal anesthesia.

Hypotensive episodes during spinal anesthesia have been treated clinically with various pressor drugs such as ephedrine, paredrinol and neosynephrin hydrochloride. The mechanism of the beneficial effects produced by these substances is often difficult to evaluate. Paredrinol [25] and neosynephrin hydrochloride [26] initiate an elevation of blood pressure as a result of increased peripheral resistance. Ephedrine apparently produces a pressor effect by increasing venous return, right auricular venous pressure and cardiac output. This pressor response to ephedrine may occur in spite of decreased or unchanged peripheral vascular resistance.[25] Therefore, on the basis of the facts outlined, ephedrine is the drug of choice to counteract the hypotension of spinal anesthesia. The clinical findings support this concept, since alleviation of the symptoms of circulatory depression is readily accomplished with ephedrine.

The problem of prophylaxis for the hypotension of high spinal anesthesia is of no less importance than treatment. A severe fall in blood pressure cannot be considered physiologic, and its occurrence and duration during anesthesia adversely affect the morbidity and mortality of the surgical procedure being completed. The selection of patients is the primary consideration. Those with circulatory disturbances will respond poorly to further embarrassment of this function. The use of oxygen to prevent hypoxia and of pressor drugs, particularly ephedrine, to maintain blood pressure within normal limits is as definitely prophylactic as therapeutic. The other factor in prophylaxis is the role of the surgeon. This has escaped emphasis in discussions on the subject. Indubitable evidence that in man who has not been operated on the fall in blood pressure does not parallel that observed during surgery points to surgical manipulations as a factor of primary consideration. The patient with high spinal anesthesia and the major portion of his vasomotor defensive mechanisms paralyzed should have the need for such response minimized. Unnecessary surgical trauma is never justified. During high spinal anesthesia it should be eliminated and in addition the unavoidable manipulations carried out with extreme care. High spinal anesthesia is not the procedure of choice for an operation which must be completed with severe loss of blood, abdominal positional changes or excessive trauma. The surgeon whose technics include rough handling of tissues, their wide exposure and other traumatic factors will not find his results improved with high spinal anesthesia despite the more uniformly convenient operating conditions.

477 First Avenue.

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ABSTRACT OF DISCUSSION

DR. SIDNEY C. WIGGIN, Boston: I agree with Dr. Papper that we have been able to control circulatory changes for the most part by the use of vasoconstrictor drugs, together with the use of many other agencies, such as preparation of the patient, recognition of variations in technic and action of different agents, chiefly maintenance of oxygenation, and minute by minute observation of the effects of the drugs and surgery with the early treatment of complications. Spinal anesthesia can be the safest and most efficient method for operations below the diaphragm in selected cases. In the relief of pain in the present worldwide conflict it will be used more than any other method, especially when it has been estimated that over 50 per cent of wounds occur below the hips. To explain satisfactorily the physiology of spinal anesthesia, we must consider the theories mentioned by Dr. Papper. Although perhaps conflicting and not complete in themselves, each theory contributes to our knowledge of the effects of spinal anesthesia on the vital centers, and structures of the body which control the physiologic functions. Thus, Seevers and Waters in 1931 described the local diffusion of procaine hydrochloride in the subarachnoid space resulting in paralysis of the accessory muscles of respiration, and they recommended oxygen for the ensuing anoxia. Nowak in 1932 demonstrated central absorption of procaine from the spinal canal by dyes introduced into the spinal fluid and isolated in the urine. He then introduced lethal doses of procaine into the veins of a series of cats and intraspinally below the second lumbar vertebra into another series and showed a similar development of toxic symptoms and death in both groups, with the detection of procaine in the urines. I agree with Dr. Papper that the most serious complications in spinal anesthesia are principally the result of the lack of individualizing the patient and the recognition of the factors related to surgery itself. Rovenstine's description of traction reflexes has clearly shown the part overstimulation of vital nerve centers plays in the disturbance of the patient's physiologic balance in spinal anesthesia and surgery.

DR. STUART C. CULLEN, Iowa City: The lack of conformity of opinion in explaining the hypotension associated with spinal anesthesia and the diametrically opposed interpretations of data obtained in studies of this subject seem to indicate an incomplete understanding of some fundamental factor. That the fundamental derangement in circulatory stability is a consequence of the absence of sympathetic control is a theory fairly well accepted. The nature of the sites of action of this control, their extent and the degree of autonomous integrity of the peripheral vascular system in the absence of sympathetic control are the real problems to be answered. Dr. Papper's theory of maintained arteriolar competence with venocapillary stagnation is logically considered. It is difficult, however, to reconcile this arteriolar competence with incompetent postarteriolar capillaries. Must one assume that sympathetic impulses are nonessential to the maintenance of tone of the arteriole and essential to the maintenance of tone in the postarteriolar capillaries? The evidence presented does not exclude relative degrees of arteriolar incompetence. By the criteria employed, such as reduced venous pressure, decreased cardiac output and increased difference in arteriovenous oxygen saturation, to establish arteriolar competence, relative degrees of arteriolar atonicity are not revealed. The moderate degrees of lowering of diastolic pressure can be interpreted to indicate some decrease in peripheral resistance due to loss of arteriolar tone. Dr. Papper has emphasized the significance of mechanical interference with the dynamics of a peripheral vascular system under the influence of spinal anesthesia. This is a contribution of much practical importance. It does not seem logical to assume that "vasomotor defense" is lodged entirely in the postarteriolar bed in view of anatomic evidence that arterioles are

richly supplied with sympathetic nerve fibers. It does seem logical, however, to assume that in the maintenance of normal tension by integration of the peripheral vascular system through the sympathetic system the arteriole, as well as the capillary bed, plays a significant role. In the absence of sympathetic integration, autonomous arteriolar control is sufficient to maintain relatively normal tension in the resting supine state, but not sufficient to effect the proper distribution of blood in other positions and in response to unusual demands.

DR. HENRY K. BEECHER, Boston: The views that Dr. Papper has presented have a considerable basis in the papers that Smith, Rovenstine, Chasis, Goldring and that group recently presented. Those papers and Dr. Papper's presentation suggest that a question might be raised here as to how far conclusions can go when based on studies of a single organ or system. I believe we all agree that it is not wise to draw many general conclusions about the circulatory effects of spinal anesthesia from observations of the circulation of the skin. We all appreciate the fallacies inherent in that, and I want to call attention to a similar question in regard to the paper presented today, and the earlier papers; namely, the hazards of drawing too many conclusions from the kidney. It is well to speak of this in the light of recent observations by Dr. R. H. Smithwick, who has found that the kidney is to some extent innervated through pathways that come from well above the level that is reached by the high spinal anesthesia of the study under discussion. The kidney innervation is certainly widespread and extensive; it may arise as high as the second or third dorsal region. Furthermore, acute denervation as accomplished with local anesthetics may not give an accurate picture of persistent denervation effects. Such studies as these should include the behavior of the kidney under various reflex stresses and strains, as Smithwick has pointed out.

DR. E. M. PAPPER, New York: In answer to Dr. Cullen I would state that the thesis maintained is that arteriolar dilatation is not an important factor in normal man, not operated on, under the standard conditions of our investigation, and that all the evidence indicates that whatever hypotension occurs is due to a fall in cardiac output, which is, in turn, attributed to failure of circulation in the postarteriolar bed. Concerning the question Dr. Cullen raised about the individual's vasomotor defense during surgery, I agree that other factors might play an important part in the hypotension during clinical surgery. In fact, that is one of the strong points of our thesis in this argument, that the patient who is operated on is a different individual from the one who is not. Since he is adequately denervated as far as the sympathetic nervous system is concerned, he cannot compensate for the changes that occur during manipulation, trauma, hemorrhage and change of position. Whether that is due to superimposed arteriolar dilatation during surgery or whether it is due to failure of arteriolar constriction beyond normal tone, I don't think we can say at the present state of our knowledge. In answer to Dr. Beecher's question, the systemic circulation has been studied with direct arterial cannulation for arterial pressure and by the ballistocardiac method for cardiac output. We are able by these methods to measure the actual cardiac output and the actual mean pressure and thus to determine the overall peripheral resistance which must lie largely in the arterioles. Therefore, the work does not rest entirely on renal blood flow but on direct observations in the general circulation.

Tuberculosis in Old Age.—It is erroneous to assume that tuberculosis occupies a subordinate position in old age. Compared with the number in the younger age groups fewer senile persons fall sick or die from the disease, but there is no percentage decrease of tuberculosis in the aged. The mortality rate of the infection for all white persons (1 to 74 years) insured by a large company for the years 1931 to 1935 was 68.4 for males and 98.6 for females. Between the ages of 20 and 24 the rate was 54.8 for men and 84.8 for women. In the group 64-74 years there was a striking rise and a reversal of sex differences, 130.5 for males and 66.7 for females.—Mueller-Deham, Albert, and Rabson, S. Milton: Internal Medicine in Old Age, Baltimore, Williams & Wilkins Company, 1942.

SPINAL ANESTHESIA

FACTORS INFLUENCING ITS SUCCESS

LEO V. HAND, M.D.
BOSTON

The success of any anesthesia is dependent on three general factors: (1) the patient and his disease,[1] (2) the choice of agent and method of administration [2] and (3) the skill and experience of the person administering the anesthesia. This is especially true when anesthesia by means of the subarachnoid route is elected.

My purpose in this paper is to mention or review some of the objective findings, observations, points in technic and corrective steps instituted that have an important influence on the success of anesthesia by the subarachnoid route. For purposes of coherence, these specific clinical factors will be presented under the following subtitles: (1) preparations of the patient including preoperative medication,[3] (2) choice of agent and method, and (3) administration of the agent and its supervision.

PREPARATION OF THE PATIENT

The preparation of a patient for spinal anesthesia not only necessitates a thorough knowledge of the objective findings which may influence its course but also includes an intimate knowledge of the patient's emotional status toward or past experience with this or allied methods of anesthesia. Patients in shock [4] are known to be poor candidates for spinal anesthesia. Recent experiences [5] among war casualities have further strengthened this observation. Patients with moderate to severe anemia tolerate the usual doses of agent poorly. Patients with anemias, cachexias or other blood dyscrasias should receive blood transfusions prior to the day of operation. Also it is inadvisable to elect spinal anesthesia in the presence of neuropathologic findings within the cerebrospinal system. Occasionally spinal pain following anesthesia has been attributed to the anesthesia when subsequent examination has revealed evidence of a concomitant neuropathologic condition.

A preoperative interview acquaints the patient with the anesthetist and the contemplated method. It also elicits valuable information from the patient as to his reactions to an anesthesia or his past experience with a similar anesthesia. Many patients are not receptive to spinal anesthesia for one of the following reasons: 1. The patient prefers to be asleep. 2. From hearsay, usually grossly exaggerated, the patient has been warned against spinal anesthesia. 3. The patient's local physician warns him against spinal anesthesia. 4. The patient has had a previous, decidedly unpleasant experience with an inadequate spinal anesthesia. 5. The patient tells the anesthetist of untoward reactions when this method was employed on a former occasion. Of these five reasons, the one requiring the most attention and investigation is the last—that is, the ques-

From the Department of Anesthesia, the Lahey Clinic.

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2. Sise, L. F.: Choice of Anesthesia, Am. J. Surg. **34:** 419-427 (Dec.) 1936.
3. Sellman, P.: Preoperative Medication, S. Clin. North America **20:** 621-631 (June) 1940.
4. Woodbridge, P. D.: Indications and Contraindications of Spinal Anesthesia, S. Clin. North America **20:** 615-620 (June) 1940.
5. Beecher, H. L.: Personal communication to the author.

tion of idiosyncrasy. The most difficult to counteract is the fourth—a "gun shy" patient. The most annoying is the careless, thoughtless or officious remarks of an inexperienced physician. The easiest to cope with is the first—the desire to be asleep.

As a result of this preoperative visit and review of objective findings, the anesthetist is better able to evaluate the anesthetic risk of the patient. Depending on this information and grade of risk, the dose of preoperative medication is determined. The doses of preoperative medication usually ordered for good risk adult patients are pantopon ⅓ grain (0.02 Gm.), scopolamine hydrobromide 1/150 grain (0.4 mg.) subcutaneously two hours before the scheduled time of operation, and soluble pentobarbital 3 grains (0.2 Gm.) by mouth one hour before the operation. The soluble pentobarbital is given by rectum when oral medication is contraindicated. Patients with this medication usually arrive in the operating suite in a drowsy or euphoric state of mind, ideal for surgery on a conscious patient. Occasionally patients show little effect from this medication; in such instances medication is reinforced just before spinal puncture with varied doses of morphine 1/12 to ⅙ grain (0.005 Gm. to 0.011 Gm.) and scopolamine hydrobromide 1/300 to 1/200 grain (0.2 to 0.3 mg.) intravenously.

CHOICE OF AGENT AND METHOD

The agent and method to be employed in spinal anesthesia depend on the contemplated operation. The more commonly employed agents are procaine hydrochloride, pontocaine hydrochloride and nupercaine. The respective indications for these three agents as employed at the Lahey Clinic have been reported in detail elsewhere.[6] Pontocaine hydrochloride combined with dextrose, as originally reported by Sise,[7] is most commonly used. By the use of the Sise technic (gravity method), the maximal concentration of the drug in the subarachnoid space is deposited at or around the nerve roots supplying the site of operation. This results in maximal concentration of anesthetic in these areas. This heavy solution with the patient in a supine position tends to result in a high sensory or posterior root anesthesia and an appreciably lower, and thus safer, motor or anterior root anesthesia.

Recent developments in the method of administration or technic have eliminated the former objection of limited or too short duration of anesthesia. Present day methods may be divided into the conventional or single dose method[8] and the continuous or fractional method[9] with repeated doses of an agent as needed. It is the opinion of the members of this department that fractional spinal anesthesia[10] will not completely supplant the conventional method of administration. In our opinion, indications for the fractional method are (1) operations in which the anticipated duration will exceed the duration usually obtained by the single dose method and (2) operations of unpredictable duration.

6. Hand, L. V., and Sise, L. F.: Nupercaine Anesthesia, Surg., Gynec. & Obst. **71**: 9-21 (July) 1940. Nicholson, M. J.; Eversole, U. H., and Hand, L. V.: Fractional Spinal Anesthesia, Am. J. Surg. **53**: 403-411 (Sept.) 1941.

7. Sise, L. F.: Pontocain-Glucose Solutions for Spinal Anesthesia, S. Clin. North America **15**: 1501-1511 (Dec.) 1935; **16**: 1707-1711 (Dec.) 1936.

8. Saklad, M.: Spinal Anesthesia, New England J. Med. **213**: 1226-1235 (Dec. 19) 1935.

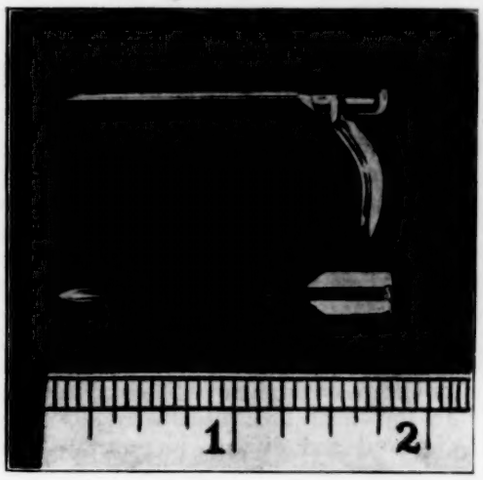
9. Lemmon, W. T.: A Method for Continuous Spinal Anesthesia, Ann. Surg. **111**: 141-144 (Jan.) 1940.

10. Hand, L. V.: Spinal Anesthesia, by Fractional (Continuous) Method of Administration, Anesth. & Analg. **121**: 189-199 (July-Aug.) 1942.

ADMINISTRATION OF AGENT AND ITS SUPERVISION

To some anesthetists the review of minor points of the technic of lumbar puncture may hold some interest. To a few it may be instructive. The administration and supervision of an agent is essentially technical and is governed by three components: (*a*) the equipment, (*b*) the agent and (*c*) the administrator.

The syringe and its size are dependent on the agent elected and the quantity deemed sufficient for anesthesia. The type and gage of needle have an influence on the success of spinal anesthesia. Clinical investigations[11] by the late Dr. Sise suggest that the gage of the needle has a definite influence on the incidence of postlumbar puncture headache. For patients with a planned, very short bed stay, that is six to twenty-four hours, we employ a No. 24 gage needle. For routine conventional spinal anesthesia we use a No. 21 gage needle. This 21 gage needle has a flexible, seamed, gold shaft and nickeloid hilt. Since its introduction we have not had a needle break within the body tissues during lumbar puncture. For fractional or continuous spinal anesthesia we use a special No. 19 gage limber nickeloid needle.



Moore introducer.

An introducer is employed to guide this flexible, soft needle through the interspinous ligament. The new introducer illustrated, devised by Dr. George C. Moore[12] on the principle of a groove director, has been an invaluable aid in facilitating accurate, speedy lumbar puncture when the flexible continuous spinal needles are used. This introducer can readily be removed without disturbing the indwelling needle. The combination of indwelling introducer and needle should be avoided. To my knowledge the only needle used for continuous spinal anesthesia broken within a patient's back was when a rigid walled introducer acted as a shearing blade when the patient was turned from a lateral flexed to a supine extended position.

When the pontocaine-dextrose technic is employed, the patient's head is always flexed so that the most dependent area of the spinal column is approximately between the second and the fourth thoracic segment. This tends to prevent upward cervical and medullary

11. Sise, L. F., and Swinton, N. W.: A Method for the Prevention of Postpuncture Headache in Cases of Low Spinal Anesthesia, S. Clin. North America **19**: 695-698 (June) 1939.

12. Moore, G. C.: Personal communication to the author.

progression of anesthesia. With this technic the upward progression of anesthesia is obtained by gravity. The patient is placed in a 10 degree Trendelenburg position for a very short period (one to two minutes). The degree of the Trendelenburg position is to be judged not by the degree of table slant but rather by the actual slant of the spinal column. An obese person with narrow shoulders and broad buttocks will actually be in a 15 degree Trendelenburg position when a table tilt is recorded at 10 degrees. It is in such instances that the complication of severe respiratory embarrassment occurs most frequently.

The usual site of election for lumbar puncture is the third lumbar interspace. In operations in which the contemplated procedure will be entirely in the upper part of the abdomen, a better concentration of anesthesia [13] is obtained and maintained when lumbar puncture is made in the second lumbar interspace. The spinal needle should not be introduced with any degree of roughness. When so employed, the usual result is not only a painful lumbar puncture but also traumatization of periosteum. Lumbar puncture in some obese persons may be a difficult procedure. In such instances the introducer or needle may be used to locate the interspace. If puncture is not obtained after one or or two attempts, the employment of geometric principles will always facilitate midline puncture. This is easily accomplished by introducing the needle toward the left side until radiating pain is elicited in the left knee, then repeating the procedure toward the right side until similar radiation of pain results in the right knee. Having thus determined lateral nerve emergence, one bisects this angle and a painless successful puncture is obtained. These steps save unnecessary, haphazard repeated attempts, usually accompanied by considerable periosteal traumatization and pain. Again, in patients requiring lumbar puncture twenty-four to forty-eight hours after encephalography or spinography, the decided diminution of spinal fluid usually results in a dura readily displaced and difficult to puncture. In such instances the following steps facilitate puncture: (*a*) a drop of fluid in the hub of the needle will be sucked in when the epidural space is entered—thus an important landmark of the proximity of the dura and (*b*) a needle with a bevel angle of less than 90 degrees and a sharp cutting point facilitates this dural penetration.

With the special needle for continuous spinal anesthesia it is advisable to persist in lumbar puncture manipulation until fluid can be aspirated readily with the patient in the supine position, even if this necessitates a repuncture. In instances in which this precaution was ignored, invariably attempts to maintain high anesthesia by subsequent injections were either difficult or unsuccessful.

The accurate determination of heights of anesthesia is an important step. It informs the anesthetist of approaching, unnecessary and potentially dangerous heights of anesthesia. It determines the adequacy of the height of anesthesia. An inadequate anesthesia without a supplemental remedy results in a disturbed patient as well as exceedingly poor operating conditions. When testing, the more accurate response is obtained by negative suggestion. For instance, it is preferable to say "You do not feel" rather than to ask "Do you feel?" The patient's response to the usual type of questioning will depend on his tolerance to pain and his emotional status. When the suggestive negative form is employed, the patient will quickly and emphatically correct you in the presence of definite pain stimuli. In patients with language difficulties or excessive medication, objective responses, particularly facial wincing to test stimuli, are good indexes of the upward progression of anesthesia.

After satisfactory anesthesia has been obtained, the clinical course is checked frequently and recorded at at least five minute intervals. From the information obtained, the anesthetist is better able to safeguard against or institute early corrective measures to combat operative complications. These observations consist in blood pressure, pulse and respiratory recordings, determination of the presence or absence of intercostal breathing and a close watch for early signs of beginning loss of anesthesia.

In all operations of a serious nature or when there is a question of long duration an intravenous infusion is started and maintained throughout the operation. This infusion affords a ready access for corrective measures, such as blood and intravenous medication, to combat certain operative complications and is a channel by which complementary intravenous agents may be employed.

COMMENT

In many operations in the upper part of the abdomen, a complementary agent,[13] either inhalation or intravenous in nature, is employed for the following reasons: The first and most important is to lessen objective response to traction stimuli, thus lessening the severity of certain potential operative complications. The second is that many patients prefer to be asleep. The third is that it permits greater freedom of discussion of the pathologic conditions and contemplated treatment.

The immediate postoperative orders for sedation and fluid are usually the responsibility of the anesthetist. He is better qualified to judge and is familiar with the physiologic state of the patient resulting both from anesthesia and from the operation.

The operative complications associated with and most likely caused by traction reflexes are appreciable falls in blood pressure with little to no pulse disturbances, usually accompanied by nausea and retching in a conscious patient. This circulatory depression is not as severe and the gastrointestinal response is eliminated with the patient asleep. In instances of nausea and retching, oxygen is routinely administered. When the blood pressure recordings approach 50 per cent of the original preanesthetic systolic levels, a vasodepressor drug is given to inhibit further falls in blood pressure and to treat the present depressed state. The pressor drug combination usually employed is an intramuscular injection of pitressin [14] 5 units and ephedrine 3/8 grain (0.024 Gm.). With this combination not only is blood pressure improved but this improvement is sustained for an appreciable period in the nature of a plateau effect.

Transfusions of whole blood plus oxygen and pressor drugs are given in instances of shock or impending shock. No substitute such as plasma or albumin is as effective as whole blood, particularly in instances of shock due to loss of blood.

Second in frequency to circulatory depression is loss of anesthesia. With the continuous spinal method this complication is eliminated. The single dose administra-

13. Hand, L. V., and Sise, L. F.: Anesthesia for Gastric Surgery, S. Clin. North America **21**: 803-815 (June) 1941.

14. Raginsky, B. B.: The Present Status of Analeptics in Anesthesia, Tr. Am. Coll. Surgeons **1**: 66-73 (July) 1938.

tion necessitates a supplementary anesthesia of sufficient depth to obtain motor relaxation. The following signs are indicative of beginning loss of anesthesia. The earliest is a vasomotor change manifested by perspiration. Next the patient complains of vague discomfort. Simultaneous with this discomfort, the abdominal viscera tend to balloon up and fill the incisional opening. The last is beginning loss of relaxation. Through inexperience or careless supervision signs of loss of anesthesia are not recognized until beginning loss of relaxation. In such instances the transition to an inhalation anesthetic results in a very stormy and disturbing period for the patient.

Occasionally spinal anesthesia may become too high, with resultant progressive respiratory signs of ascending anesthesia. These progressive signs are absent intercostal to reversed intercostal action accompanied by suprasternal notch tugging and a progressive increase in accessory respiratory muscle action to absence of respiration. The treatment of this complication will depend on the degree of respiratory involvement. The mental state of the patient plus the objective degree of paralysis usually influence further procedure. Usually light supplementary anesthesia will suffice to alleviate the disturbed mental state of the patient. If the patient is kept abundantly supplied with oxygen, it is remarkable how little disturbance is caused him even by a considerable degree of intercostal paralysis. In instances of complete respiratory paralysis it is necessary to resort to passive breathing and to insure a patent and clear airway. A patent airway is best obtained by means of intratracheal intubation. The duration of intercostal paralysis is dependent entirely on the duration of anesthesia.

No method of anesthesia can excel spinal anesthesia in regard to the relaxation obtained, especially in abdominal surgery. Certain physiologic, pharmacologic and technical precautions or specific factors influence its success.

605 Commonwealth Avenue.

ABSTRACT OF DISCUSSION

DR. R. J. WHITACRE, East Cleveland, Ohio: Dr. Hand's presentation should do much to stimulate our interest in obtaining a better understanding of certain factors essential to the safe and satisfactory use of spinal anesthesia. The relatively high morbidity and mortality rates of spinal anesthesia are inconsistent with the impression that spinal anesthesia is a simple mechanical process of injecting drugs into the subarachnoid space. It requires as much experience, knowledge and skill as any other type of anesthesia. The progress in spinal anesthesia has been so rapid that the number of complications can be materially reduced if the available information is properly utilized. Dr. Hand has called attention to the advisability of using less than the ordinary dose of the anesthetic agent for the impaired risk patient. Although this factor is generally recognized in inhalation anesthesia, it is frequently ignored in estimating the dose of the spinal anesthetic. Certain other cases such as full term pregnancy also require less than the ordinary dose. The concentration of the anesthetic solution when injected into the spinal canal must be rigidly controlled. With agents of different potencies it is necessary to vary not only the dose but also the concentration of the drug. I should like to emphasize the need of preventing hypoxia during spinal anesthesia. Dr. Hand has stressed the means of maintaining circulation so that an adequate supply of oxygen may be transmitted from the lungs to the tissues. Simultaneous circulatory and respiratory depression occurs so frequently during spinal anesthesia that one cannot assume that every patient is adequately oxygenated when breathing air. To many patients it is of advantage to administer oxygen with a gas machine. This provides a positive means of not only increasing the tension of oxygen but also evaluating the patient's actual respiratory exchange at all times. This is a more reliable index of pulmonary efficiency than the presence or absence of intercostal activity. The three factors adequate oxygen in the inspired atmosphere, adequate pulmonary ventilation and adequate circulation require particular attention during spinal anesthesia. When intentionally supplementing spinal anesthesia, it is frequently possible in selected cases to use less than the usual dose of the agent. This is another important means of increasing the safety of spinal anesthesia. In reference to continuous spinal anesthesia it is reasonable to say that the time or length of operation is not the only indication. It is equally important to use continuous spinal anesthesia for certain poor risk patients regardless of the duration of the operation.

DR. VIRGINIA APGAR, New York: Dr. Hand has summarized well the main problems concerned with the proper management of a patient under spinal anesthesia. There are three points on which I wish to comment: 1. The method he describes to locate the spinal canal in difficult situations depends on the production of paresthesia. I think any regional method which relies on paresthesia as a definite landmark is to be discouraged. It is bad enough to produce it accidentally. May I suggest in such cases that entrance to the spinal canal by way of the paravertebral route, passing the needle cephalad to the transverse process, is frequently easier than by the midline approach and is usually not accompanied by pain. 2. One reliable method for determining the descending level of spinal anesthesia has been implied by Dr. Hand but not mentioned specifically. As with all technics a careful observation and interpretation of respiration is indispensable. The encroachment of the intestine on the operative field after it has supposedly been well packed off is due to the increased tidal volume of the patient as well as to the loss of the hypertonic state. In my experience an increase in respiratory exchange usually precedes vasomotor changes or complaints by the patients or surgeon. 3. No one can predict accurately the future place of the continuous spinal method. I have a feeling that its use will be more widespread than suggested by Dr. Hand. In general I believe that it will be used in cases of spinal anesthesia in which 100 mg. of procaine hydrochloride is not considered sufficient. We are permitted to use the least toxic regional drug—at present procaine—in all cases, and in much more accurate and individualized doses. The complete absence of the most serious spinal complication, respiratory paralysis, overweighs the occasional hypotensive state, which is difficult to control.

DR. F. ELMORE HUBBARD, Montclair, N. J.: I want to ask Dr. Hand the name of the groove introducer and where one can procure it.

DR. GEORGE C. MOORE, Boston: Regarding the grooved introducer, I want to say that it has been found to be just as satisfactory to use it with a small needle, 21 or 22 gage, as with the needle for continuous spinal anesthesia. With the smaller needle, of course, it may or may not be removed. I am not sure I am entitled to priority in originating it because I learned this morning that Dr. Batten of the Methodist Hospital of Brooklyn has devised a somewhat similar instrument. I haven't seen his, so I can't describe it. If I may answer Dr. Hubbard, the McGregor Instrument Company of Needham, Mass., is making the instrument.

DR. LEO V. HAND, Boston: In regard to Dr. Apgar's suggestions, I agree with her relative to the method of paresthesias in developing anesthesia. That is not advisable, but frequently of necessity we employ it. For a particularly obese individual and when I do not care to have him sit up or follow the usual procedure it frequently proves in my hands to be a quicker method of locating the spinal canal. As to the future of continuous spinal anesthesia, that is a question. In the hands of surgeons a continuous spinal anesthetic may supplant the conventional dose method. I fear the situation may arise when all they have to do is turn to the nurse or intern, or whoever is supervising, and say "More relaxation" irrespective of the physiologic state of the patient.

MICROAEROPHILIC HEMOLYTIC STREPTOCOCCUS INFECTION CAUSING DESTRUCTION OF NOSE

MAURICE J. COSTELLO, M.D.
NEW YORK

Prior to 1924, hemolytic streptococcus gangrene was reported under various clinical titles which included contributions by Seeman,[1] by Hawkins[2] and by Stirling[3] under the title of "gangrene of the scrotum and penis" and as "streptococcus scrotal and penile gangrene" by Campbell.[4] In 1924 Frank L. Meleney[5] reported 20 cases of hemolytic streptococcus gangrene from the clinic of the Peking Union Medical College in China, where he stated that the disease was fairly common. Fedden[6] in 1909 and Pfanner[7] in 1918 described cases of acute infective streptococcus gangrene of the extremities which Meleney thought were similar to those he studied in the Orient.

Since 1924 reports have appeared on the clinical recognition, on the bacteriologic studies, and on the treatment of an infection from which it is to be differentiated, namely that caused by the microaerophilic hemolytic streptococcus. The majority of these articles are the lucid contributions of Meleney and his co-workers. Unfortunately, microaerophilic hemolytic streptococcus infection of the skin is seldom diagnosed early because of ignorance of its existence—the disease is admittedly rare—and also because of failure to order anaerobic as well as aerobic cultures of all infections of the skin of an obscure nature.

The request for anaerobic culture studies is so infrequent that many bacteriologic laboratories are not equipped to perform them properly.[8] The causative organism of this infection has been called microaerophilic because it grows best under slightly reduced oxygen tension.[9] It is for this reason that specimens for bacteriologic study should be taken from the sinuses and the undermined edges of the wound.

From a study of the literature it appears that any portion of the skin may be affected by this disease, but it occurs most frequently on the extremities, especially in men. The perineum, scrotum and penis are often affected. This is probably due to the proximity of these organs to the anal orifice, the hemolytic streptococcus being often found in the intestinal tract.[10]

Meleney's clinical description of this disease, repeated in all his writings, should make it as recognizable as erysipelas, from which it is to be differentiated. His further studies on the bacteriology of the causative organism—the microaerophilic hemolytic streptococcus—should make confirmation of the diagnosis a relatively simple matter, if this infection is kept in mind. Effective treatment then can be instituted promptly, preventing suffering, loss of time, money and life itself.

The organisms causing this infection may enter the body following superficial injury to the skin, a scratch, an abrasion, a boil, a herpetic lesion, a hypodermic injection, a severe injury or a minor or major surgical procedure.[11]

Prolonged suppuration leads to the development of ulcers having undermined borders and sinuses which burrow into the deep tissues. Muscle and bone are not often affected unless injured at the time of the original trauma. Severe hidradenitis suppurativa of long standing involving the axillas and inguinal regions may be complicated by this type of infection. Several of the cases reported suggest this possibility.[10]

This disease may be mistaken for erysipelas, cellulitis, pyoderma gangrenosum, tertiary syphilis, tuberculosis and varicose ulcers when it occurs on the extremities. When the lesions occur on the face and especially around the nose, almost invariably a diagnosis of syphilis, tuberculosis, carcinoma or rhinoscleroma is entertained. It is during this period of mistaken diagnosis that valuable time is lost and mutilating destruction occurs.

The case I am about to report exemplifies the difficulty in diagnosing this serious infection.

REPORT OF CASE

M. F., a woman aged 59, when first seen by me on Dec. 20, 1937, had an ulcer on the right side of the nasal septum and the floor of the right nasal cavity for thirteen months, which had increased in extent in spite of many types of local and general therapy. The extensive ulceration involved the mucous membrane of both nasal cavities with an irregular vertical perforation of the anterior portion of the nasal septum. The floor of the ulcer was covered with tenacious seropurulent exudate. The skin of the bulbous portion of the nose was dull red, edematous and tender on pressure. There was no pain, but numbness was a prominent feature. The redness faded gradually into the normal skin. During the first weeks of observation by me the patient had a moderately elevated temperature, 101-102 F., had frequent sweats while sleeping and complained of fatigue and shortness of breath. Frequent microscopic examinations of smears did not show Vincent's organisms or tubercle bacilli. The Gram stain showed occasional gram positive cocci which resembled pneumococci. Cultures showed hemolytic streptococci. The Wassermann reaction of the blood and the Kline precipitation test were negative on three different occasions. The sugar content of the blood was 114 mg. per hundred cubic centimeters. Urinalyses showed no abnormality, and the leukocyte count was between 12,000 and 16,000 on a number of occasions. Roentgenograms of the maxillary bones showed no abnormality. A roentgenographic study of the chest revealed numerous calcifications and a general peribronchial thickening throughout each lung, particularly in the inferior lobe of the right lung. Several biopsies were performed. The first showed "chronic suppurative inflammation." A specimen of the nasal mucous membrane showed a "hyperkeratotic papilloma," and a specimen from the skin showed "hyperplastic inflammatory tissue."

During the first six weeks the patient received five intravenous injections of neoarsphenamine each 0.45 Gm., two of bismarsen and daily oral administration of 4 fluidrachms (15 cc.) of saturated solution of potassium iodide. There was no improvement in the lesion during this treatment. Local therapy consisted of irrigations with solution of boric acid and 1 per cent aqueous solution of brilliant green and 1 per cent aqueous solution of methylrosaniline.

The patient was tested with old tuberculin by graded intradermal injections on the forearms in dilutions of 1 : 100,000, 1 : 1,000,000 and 1 : 10,000,000. The areas of the skin injected became erythematous and swollen, and in forty-eight hours

Read before the Section on Dermatology and Syphilology at the Ninety-Third Annual Session of the American Medical Association, Atlantic City, N. J., June 12, 1942.

1. Seeman, D.: Ztschr. f. Chir. **150:** 145, 1919.
2. Hawkins, J. A.: Mil. Surgeon **50:** 419 (April) 1922.
3. Stirling, W. C., Jr.: Case of Gangrene of Scrotum and Penis, J. A. M. A. **80:** 622 (March 3) 1923.
4. Campbell, M. F.: Surg., Gynec. & Obst. **34:** 780 (June) 1922.
5. Meleney, Frank L.: Hemolytic Streptococcus Gangrene, Arch. Surg. **9:** 317-364 (Sept.) 1924.
6. Fedden, W. F.: Proc. Roy. Soc. Med. **2:** 213, pt. 1, 1909.
7. Pfanner, W.: Deutsche Ztschr. f. Chir. **144:** 108, 1918.
8. Meleney, Frank L.: Hemolytic Streptococcus Gangrene, J. A. M. A. **92:** 2009-2012 (June 15) 1929.
9. Meleney, Frank L., and Johnson, B. A.: Surgery **1:** 169, 1937.
10. Meleney, Frank L., and Harvey, Harold D.: Ann. Surg. **110:** 1067-1094 (Dec.) 1939.
11. Shallow, Thomas A.; Fry, Kenneth E., and Pulaski, Edwin J.: Surg., Gynec. & Obst. **70:** 987-995 (June) 1940. Meleney and Harvey.[10]

a bulla developed at the site of each injection. These bullae were followed by ulcerations, which were of equal size despite the difference in dilution of tuberculin.

I presented the patient at the Manhattan Dermatologic Society in February 1938 with the diagnosis of pyogenic ulceration of the nose.[12]

She was again presented before the same society in April 1939 because of an exacerbation of the infection.[13] The infection had been dormant from June 1938 to January 1939. The period of remission was ascribed to the therapeutic effect of the iodides or tuberculin.

At that time she had an extension of the ulceration of both nasal cavities with complete destruction of the lower half of the septum. The skin of the bulbous portion of the nose was dusky red, swollen and tender, and the involved area was not sharply marginated. An infectious eczematoid dermatitis appeared on the upper lip. During the following five months the infectious process destroyed the columella. The patient was again given large doses of the saturated solution of potassium iodide, this time without benefit. She received adequate doses of sulfanilamide, azosulfamide and sulfapyridine without favorable effect on the infection. Prior to the onset of the disease the patient's general health had always been good except for an eruption on the palmar surfaces of the tips of the fingers during the winters of 1903, 1906, 1912 and 1913, which consisted of deep indolent ulcerations, probably papulonecrotic tuberculid. The resulting scars are still visible.

After the diagnosis of microaerophilic hemolytic streptococcus infection was confirmed by the bacteriologic studies performed by Dr. Frank L. Meleney, the application of zinc peroxide cream caused gradual arrest of the infection. When the patient was last seen the disease process appeared to be controlled.

COMMENT

Treatment should be instituted immediately after the clinical diagnosis of microaerophilic hemolytic streptococcus infection is confirmed by proper anaerobic bacteriologic studies. If the infection involves a small area it should, if possible, be excised and the operative wound should then be treated with zinc peroxide paste. Skin grafting should be performed if necessary after the infection has been eradicated. Meleney advises surgical incision to encourage adequate drainage and relief of tension of the swollen tissues, especially if the infection involves the extremities. Forty per cent zinc peroxide cream is made by mixing equal amounts of the potent sterilized powder and distilled water.[14] Since the microaerophilic hemolytic streptococcus is an anaerobic organism living in the recesses of the burrowing ulcers and the undermined edges of the wound, zinc peroxide cream must be applied thoroughly to these areas. Every part of the infected surface must be in continuous contact with the medicament. Since not all lots of the powder are effective, they must be tested for potency,[15] as the powder is therapeutically efficient only by virtue of its ability to produce oxygen when it is in contact with water. When the infected area is treated with the paste, it should be covered with wet gauze to insure constant liberation of oxygen. The gauze in turn should be widely covered with zinc peroxide ointment.. The cream should never be permitted to become dry.

The sulfonamide drugs have been somewhat effective in combating this infection if administered early, before fibrosis prevents the necessary contact with the organisms.[10] Too much reliance must not be placed on them if after a short trial the advancing disease warrants intelligent surgical intervention.

12. Costello, Maurice J.: A Case for Diagnosis (Pyogenic Ulceration of the Nose), Arch. Dermat. & Syph. **38**: 106-107 (July) 1938.
13. Costello, Maurice J.: Tuberculous Ulceration of the Nose, Arch. Dermat. & Syph. **40**: 1062-1063 (Dec.) 1939.
14. Meleney, Frank L., and Johnson, Balbina: Surg., Gynec. & Obst. **64**: 387-392 (Feb. 15) 1937.
15. Meleney, Frank L., in Nelson New Loose-Leaf Surgery, chapter V-B, pp. 476K—476.

SUMMARY AND CONCLUSIONS

1. A case of microaerophilic hemolytic streptococcus infection causing destruction of the nose was observed.
2. Infections of this type may persist for an indefinite period before their true causation is determined because of remissions which are erroneously attributed to various forms of therapy.
3. Anaerobic as well as aerobic bacteriologic studies should be made as a means of arriving at a correct diagnosis early in the course of the disease.
4. Treatment by excision, incision and zinc peroxide cream is the best means of managing this serious infection.

140 East Fifty-Fourth Street.

ABSTRACT OF DISCUSSION

DR. FRANK L. MELENEY, New York: I did not realize until Dr. Costello's paper was received a few days ago that he had confused the hemolytic streptococcus gangrene, which I saw frequently in China and described in 1924 in the *Archives of Surgery*, with the undermining, burrowing, chronic ulcer due to the microaerophilic hemolytic streptococcus, which I have described more recently. This gives me the opportunity to point out the fundamental differences in the two, which should be clearly differentiated. This case falls into the microaerophilic hemolytic streptococcus undermining ulcer group. The hemolytic streptococcus gangrene is an acute, fulminating, rapidly extending infection of the subcutaneous tissues. The pathognomonic sign of this disease is a purplish area in the center of an extensive erythema. This appears on the fourth or fifth day and goes on rapidly to gangrene. The infection spreads in the subcutaneous tissues, producing an extensive slough of the subcutaneous fat, but it does not spread down into the deeper tissues. This is due to an aerobic hemolytic streptococcus. Probably there is an element of hypersensitivity in this infection, which may be the explanation for its appearing more frequently in China than in this country. In the last eighteen years I have seen fewer than fifteen of these infections. The chronic, undermining, burrowing ulcer, on the other hand, is a slowly developing chronic infection, characterized by ulceration of the skin without gangrene. It not only spreads in the subcutaneous tissues but burrows down along the muscles and along lymphatic channels, and it frequently gets into bone. When this happens it is very difficult to eradicate. It frequently erodes into blood vessels, and death may ensue from severe secondary hemorrhage. Zinc peroxide is not effective in the acute hemolytic streptococcus gangrene because the extent of inflammation in the subcutaneous slough prevents contact with the periphery of the infection. In the treatment of this disease the sulfonamides should be used in maximum doses and incision made beyond the area of subcutaneous tissue involvement, followed by treatment with diluted solution of sodium hypochlorite to aid in the liquefaction of slough. With the chronic, undermining ulcer the sulfonamides are not as effective and here the treatment of choice is zinc peroxide. The two may be combined if the drug is tolerated. If the undermining is so extensive as to prevent adequate contact with zinc peroxide, the underlying tissues must be removed by preliminary operation. Another condition which is sometimes confused with both of these lesions is the progressive bacterial synergistic gangrene, which is less acute than the hemolytic streptococcus gangrene but more rapid in its spread than the chronic, undermining burrowing ulcer. This is due, as I have shown, to the symbiotic action of the microaerophilic nonhemolytic streptococcus and Staphylococcus aureus.

DR. LOUIS A. BRUNSTING, Rochester, Minn.: In describing the character of these ulcers with their burrowing qualities and liquefying necrosis, I believe the use of the term "gangrene" is justifiable. Some of the earliest descriptions of these pyogenic

ulcerations are recorded in the Medical History of the Civil War. Infections occurred at the sites of wounds and amputations in debilitated individuals under conditions of poor hygiene. The various types of gangrenous ulcerations described by Meleney and others can be made out in the earlier writings, but with the lack of present day bacteriologic knowledge there was no systematic classification. When these lesions occur in the axillas and in the region of the genitalia and the perineum they are apt to be based on the condition known as hidradenitis suppurativa. In some instances conservative treatment with the use of antiseptics and roentgen therapy is sufficient, but when there is extending infection over a considerable site it is better to excise the field and apply skin grafts. I have been interested particularly in the type of burrowing infection called pyoderma gangrenosum, which occurs chiefly in the patient who is debilitated by chronic ulcerative colitis. In those patients the bacteriologic findings are variable, including either hemolytic streptococci or staphylococci or both. Many times the abscesses are sterile, especially when they occur at the site of an injection of vaccine or bruise, which leads me to believe that there is an element of hypersensitivity of the skin of such patients. As a general rule there is no response to treatment of any type unless the widespread infection in the colon is brought under control by attention to the general health of the patient. The use of multiple blood transfusions and repeated courses of the milder sulfonamide drugs is a helpful adjunct to the building up of the general resistance.

DR. MORRIS H. GOODMAN, Baltimore: Ulcers of the type described by Dr. Meleney should be differentiated from an ulcer which I first described and reported in THE JOURNAL, Oct. 15, 1938 with the designation chronic streptococcic ulcer of the skin. I have seen a number of cases since the date of my original report, and my observations have been confirmed by others, principally by Taylor (*ibid.*, April 4, 1942), who treated 31 cases. The lesion which I described makes its appearance following a slight injury in the form of a reddish, well defined edematous area usually on the extremities and soon ulcerates. The ulcer slowly enlarges and persists as a chronic low grade process. The borders are red and edematous and more or less tender, and the edge is somewhat boggy and frequently undermined to a slight degree. The base of the ulcer shows a fairly intact granulation tissue, and a copious serous exudate is usually present. Taylor confirmed the impression that the ulcer which I described represents a distinct disease entity quite different from the chronic undermining and burrowing ulcers discussed by Dr. Meleney. Aside from a low grade transitory lymphadentitis, the ulcers of my description are unaccompanied by any systemic effects. Dr. Meleney has stated that in his cases in the early stages one recovers an aerobic streptococcus but later this organism develops anaerobic properties. In the chronic streptococcic ulcers of the skin which I described, the organism is a beta hemolytic streptococcus which is grown in pure culture under aerobic conditions throughout their entire course, which ranged in duration, in 6 cases which I recently observed, from three months to one and a half years. In the ulcers which I described, the use of any special local treatment is unnecessary because response to sulfanilamide, as emphasized in Taylor's report and in mine, is prompt and excellent.

DR. MAURICE J. COSTELLO, New York: This patient was seen by a number of dermatologists, otolaryngologists and surgeons, all of whom failed to entertain the diagnosis as presented. The difficulty was further enhanced by the fact that this lesion occurred on the nose, which, as far as I can tell from the literature, is an extremely unusual location. Dr. Meleney has frequently stressed the importance of the early clinical recognition, confirmed by anaerobic cultures, before secondary organisms appear which make it more difficult to evaluate the role played by each. It is also important to differentiate this from tuberculosis, syphilis and carcinoma, which it simulates. Frequently the dermatologist is the first to see this type of case and I hope in the future will probably be the first one to recognize it. I thank Dr. Meleney and Dr. Brunsting for discussing this paper, and I will make the correction that Dr. Meleney referred to at the outset.

Clinical Notes, Suggestions and New Instruments

RESULTS WITH LOCAL HEATING IN PELVIC INFLAMMATORY DISEASES

CAPTAIN JOHN R. UPTON
MEDICAL SECTION, AIR CORPS, UNITED STATES ARMY
AND
GRACE BENSON, R.P.T.T., SAN FRANCISCO

We are presenting the results of heating tissue locally in the treatment of pelvic inflammatory diseases. The types of apparatus used consisted of the Elliott machine, the short wave machine and the conventional diathermy machine. One hundred carefully selected patients were taken for the study. The three most prevalent factors causing the pelvic conditions were gonorrhea, postabortal infections and postoperative complications. Our aim was not to "sterilize" the pelvis of gonorrheal organisms by long continued high temperatures but to assist in the resolution and absorption of inflammatory tissue in all chronic pelvic inflammations.

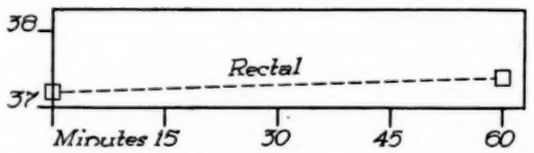


Chart 1.—Short wave diathermy: pad method. This graph shows the greatest change in temperature recorded by use of external pads. The majority of patients taking this type of treatment terminated their hour of therapy with a rectal temperature lower than that at the beginning of treatment. The recording is of a woman aged 30 whose chief complaint was pain in the suprapubic region radiating down the anterior aspects of both thighs. In 1930 an appendectomy had been performed; several years later she was operated on again for the release of adhesions, and a right salpingectomy and puncture of bilateral cysts on ovaries were executed. The diagnosis was extensive postoperative adhesions. Results from the diathermy were quite good. Relief from pain and a much freer pelvic cavity resulted. The patient was last seen in August 1938.

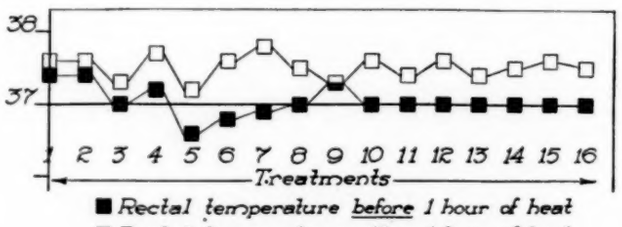

38
37
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
Treatments
Rectal temperature before 1 hour of heat
Rectal temperature after 1 hour of heat

Chart 2.—Results of sixteen successive treatments with short wave diathermy, pad method. These were carried out on the patient described in chart 1. If, as is generally thought, a moderately high temperature plays a dominant role in the treatment of an inflammatory disease of the pelvis, then this patient derived little benefit. The clinical result, however, was satisfactory, as has been pointed out.

The principal aim of any piece of therapeutic apparatus is to attempt to heal tissue and not to kill it or render the cells incapable of regeneration from disease processes or of further physiologic growth. Roentgen rays if improperly used are capable of irreparable damage to tissues, but placed in competent hands they are of inestimable value. The same is true of diathermy.

For the sake of brevity, the charts will show the results obtained and the comparisons between the three methods used. In the evaluation of such records many facts must be sifted and segregated. Several histories were excluded from this study because in our opinion the diagnosis was incorrect. For example, a woman had a retrodisplaced uterus in the third degree position. When we examined her after her first treatment we were able to bring the uterus into position quite readily, and with the help of a pessary an excellent result has been obtained. Naturally we feel that this case and similar ones should not be included in the small series presented here.

From the Department of Gynecology and the Department of Physical Therapy, University of California Hospital.

Surgical intervention is still the only method used to eradicate the results in all too many women who show pelvic disorders as the aftermath of some infection. We cannot stress too strongly the fact that if surgery only has been resorted to then the best interests of the patient have not been served. Quite frequently when a younger woman has been operated on for the usual pelvic sequelae of a gonococcic infection, the surgeon must of necessity remove several structures which are necessary to the generative system, and frequently a "clean sweep" is the result. Once tubes or ovaries are removed, the woman becomes barren soil so far as the reproductive phase is concerned. This is a particularly significant fact when we say that the great majority of our patients were under 30 years of age, i. e., in the full maturity of their reproductive cycle. This should clarify the allocation of responsibility, for if the age group fell more closely to the menopausal line there might be more reason for an operative termination of the processes of the pelvic disorder. However, we are still faced with the painful truth that the majority of these pelvic conditions are the result of a gonorrheal infection and that the highest incidence for this infection falls between the eighteenth and the twenty-fourth year. Our duty is quite clear. We should constantly seek to eradicate the inflammatory infection due to some youthful indiscretion on the part of the female and still try to maintain the reproductive processes intact, so that fertilization may later ensue and a healthy baby and mother be the ultimate happy outcome. The other two causal agents that make up the impressive triad responsible for so much pelvic trouble are postoperative adhesions and disorders and postabortal complications.

The degree and extent of a pelvic inflammation appears to have little relationship to the pain suffered. Quite frequently a woman presents a pelvis filled with inflammatory masses and yet does not complain of severe discomfort, while some slight motion to the cervix in another patient showing very little reaction causes decided pain. Different causative invading organisms, different sites attached and different stages of the infectious process must all be evaluated. The threshold for pain tolerance likewise varies considerably in different women. However, we believe that, other factors being equal, we obtain better results when the pelvic cellular reaction is minimal even though the pain experienced may be severe. The greater the inflammatory masses present, the longer time perforce must the diathermic measures be continued. Absorption and resolution of exudate takes time, and if there is a purulent condition present the time factor will of necessity be prolonged. However, the presence of accumulations of pus in the pelvis does not contraindicate diathermy and certainly does not presage a failure for the method. An acute abscess in the cul-de-sac is treated best by colpotomy drainage. As a general statement we can say that our results show that postabortal and gonorrheal infections do remarkably well under diathermy but that postoperative complications do not respond so readily.

One must be on guard for evidences of psychic trauma in women presenting pelvic symptoms. Particularly is this mental imbalance seen in the postoperative patients who have not been aided by the first operation. Several patients in our small series have had notations made in their charts by the psychiatrists to the effect that further surgical intervention might have a permanent effect on the already imperfectly functioning nervous system. We have all seen women who constantly besiege the doctor to operate on them when their real complaints might better have been dispelled by a psychiatrist. Our modern, complex, rapidly moving environment takes its toll of human economy, and women frequently show their disharmony to this rushing age by vague pelvic distress. The uncertainties of wartime, with the resultant disruption of family life, has now imposed a further strain on the human system.

There are many men who would withhold diathermic measures in chronic conditions of the pelvis and would use it only in cases of subacute involvement. We know that many

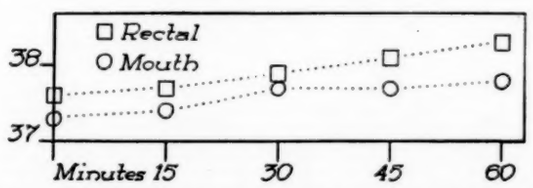


Chart 3.—Short wave diathermy: cable method. The cable was spaced completely around the pelvis. Patients taking this type of treatment complained about the generalized heating of the body. A woman aged 23 whose temperatures are charted had been subjected to three operations. An appendectomy was performed in 1937; a sinus tract which developed was explored several months later, and in 1938 a pus sac in the pelvis and the sinus tract were removed. The left ureter was constricted by the inflammatory mass and a hydroureter resulted. The diagnosis was massive postoperative and infectional adhesions and the development of a hydroureter on the left side. The patient was discharged from the gynecologic and genitourinary clinics after twelve treatments and has not been seen for four months.

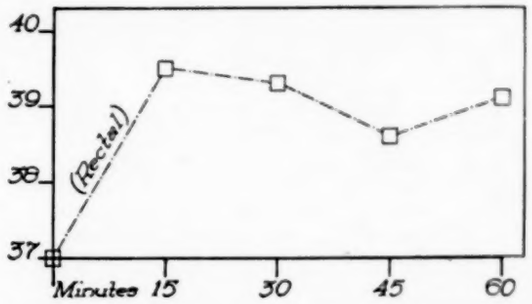


Chart 4.—Elliott treatment. A more pronounced temperature rise is seen than in the preceding charts with other methods. Frequently, however, the treatments had to be postponed because of vaginal burns sustained during the administration. If a bubble of air becomes trapped in the rubber applicator owing to the necessary manipulation incident to the pressure and suction changes, the chances of the underlying vaginal tissue sustaining a burn are increased. The method is not so easily carried out as with the conventional diathermy, and certainly more pain is experienced by the patient. Patients with intact hymens are unable to take this form of therapy. End results generally were satisfactory.

Complete Temperature Chart in Series of Twelve Treatments

Conventional diathermy approximately 2,100 milliamperes of current dispersed through 60 square inch metal plates and Chapman type vaginal electrode carrying thermometer.

Patient B, aged 26 years.

	Oral					Rectal					Vaginal				
Date	0', I	15, II	30, III	45, IV	1 Hr., V	0', I	15, II	30, III	45, IV	1 Hr., V	0', I	15, II	30, III	45, IV	1 Hr., V
July 28.....	37	37.3	37.5	—*	—*	37.5	39.4	39.7	—*	—*	—	41.7	41.1	—*	—*
July 31.....	36.8	37.5	37.7	37.8	37.8	37.5	41.8	41.8	40.5	40.8	—	42.3	41.7	42.3	42.3
August 3.....	37.1	37.6	37.8	37.9	37.9	37.5	40.5	40.7	40.9	40.7	—	42.9	42.3	42.9	41.7
August 7.....	37.1	37.5	37.7	37.8	37.8	37.7	41.3	40.6	40.2	40.8	—	42.3	41.7	42.3	42.3
August 17.....	37.1	37.3	37.4	37.3	37.3	37.3	41.8	41.9	40.2	40.5	—	41.7	41.7	41.1	41.1
August 21.....	37.2	37.2	37.6	37.7	37.7	37.3	40	37.6	40.7	41.5	—	41.7	41.7	41.7	41.7
August 24.....	37	37.3	37.5	37.6	37.6	37.3	40.5	40.3	40.7	40.1	—	42.3	41.7	41.7	41.7
August 28.....	37	37.5	37.6	37.7	37.7	37.5	41.7	41.3	41.1	40.7	—	41.1	41.7	41.7	41.7
August 31.....	37.3	37.3	37.6	37.6	37.6	37.4	39.7	39.1	40	40.4	—	41.1	42.3	42.3	43
September 11...	36.6	37	37.2	37.4	37.4	37.3	39.4	40	41	41	—	41.7	41.1	41.7	41.1
September 14...	37	37	37.1	37.5	37.5	37.1	39.8	40.3	40.3	40.3	—	41.1	41.1	41.1	41.7
September 18...	37	37.1	37.4	37.5	37.5	37.3	40.9	41.2	41.1	41.1	—	42.3	41.7	42.3	41.1
Series mean.....	37.0	37.3	37.5	37.4	37.6	37.5	40.6	40.4	40.6	40.7	—	41.8	41.6	41.9	41.8

* First treatment 30 minutes only.

chronic disorders of the pelvis have been aided materially, and we have seen some old infections literally melt away under treatment. Clinically, however, the chronic condition is more stubborn of cure than the subacute, and a longer series of treatments must be anticipated. Some patients, it is true, cannot be helped at all, and it is these who must derive aid from surgery.

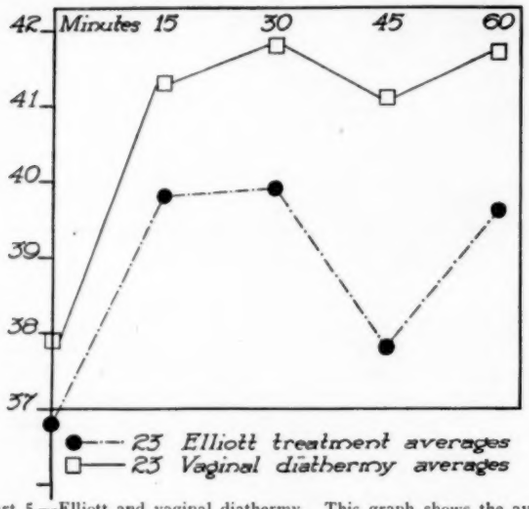


Chart 5.—Elliott and vaginal diathermy. This graph shows the average temperature of a patient who presented herself with a subacute vaginal gonorrhead infection. The Elliott machine was used first, and then vaginal diathermy was used for the second series of treatments. There is a difference of approximately 2 degrees centigrade between the two methods. Asked which treatment she preferred, she emphatically declared in favor of the vaginal diathermy. The clinical response to the Elliott machine was excellent for a while, but later on hydrosalpinx developed on the left side which under the vaginal diathermy responded extremely well. To date she has been free of symptoms.

Such important details as building the patients up physically so that the tired bodily defenses can best take advantage of the assistance offered should really not need stressing, but most of the patients with such infection fall in the poorly nourished stratum of society, and their resistance is quite low. In most instances it is found that there are several unrelated factors, all of which tend to provoke and aggravate the debilitated state of the patient. The most frequent conditions encountered outside of the pelvic infections proper were abscessed teeth, infected tonsils, chronic constipation, varicose veins, visceroptosis, malnutrition, poor posture, anemia and various stages of avitaminosis. We firmly believe that a complete general examination is imperative, for only by irradication of such nagging conditions and foci of infection can one hope to obtain amelioration of the larger issue. Chemotherapy, referring particularly to the sulfonamide derivatives, should be adequately used; occasions arise in which these drugs can be used to advantage during treatment by diathermy.

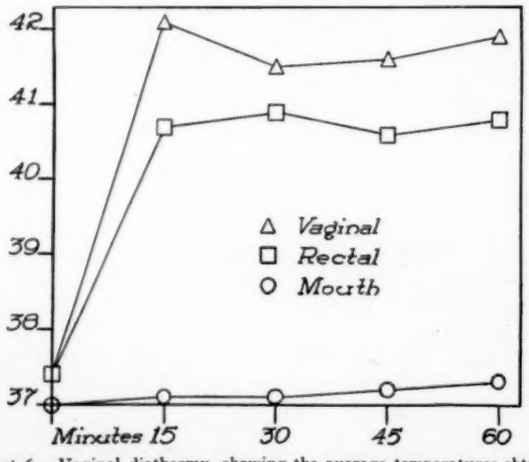


Chart 6.—Vaginal diathermy, showing the average temperatures obtained. Vaginal, rectal and mouth temperatures were recorded. Treatment by this method was smooth, with only an infrequent complaint being made about the treatment causing vaginal pain. There was a local sensation of warmness as contrasted with a generalized sense of heat when the short wave pad or cable was utilized. In treating 58 women with this technic we had 10 clinical failures, 6 for postoperative complications. Forty of the 58 patients were definitely helped by the treatment, and 24 showed a decided decrease in the size of the pelvic inflammatory exudate. There were 8 clinically cured (the criterion being complete absence from pain and a pelvis free from inflammatory exudate.) Of these 8, only 1 had a postoperative complication. Four women became pregnant and carried safely through to term and delivered without mishap.

The accompanying graphs represent a composite picture of the patients treated. The women were attended by the same technician (G. B.), so that uniformity of treatment was established and a more accurate check made possible. Follow-up examinations were likewise made by one of us (J. R. U.), and progress notes were standardized as far as possible.

SUMMARY AND CONCLUSIONS

1. Local pelvic heating should be used more extensively in the treatment of subacute and chronic pelvic inflammatory diseases.

2. Surgery should be withheld until more conservative measures have been given a trial.

3. The ideal outcome would be complete absorption of the inflammatory tissue, leaving the patient capable of reproduction and able to carry through to term.

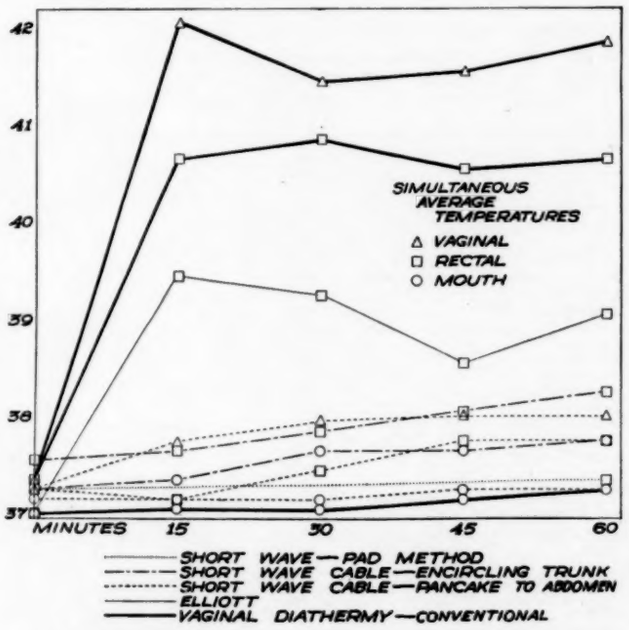


Chart 7.—Composite set of graphs illustrating the greatly varying range of temperature readings obtained by the use of the preceding methods and in addition by the use of the short wave cable in the form of a pancake on the abdomen.

4. The best clinical results were obtained with the conventional diathery for which the vaginal electrode was used.

5. The best clinical results were obtained when a moderately high temperature was sustained.

6. Short wave diathermy with the vaginal electrode gave equally good results; fair effects were noted with the pad or coil method.

7. We encountered a number of vaginal burns when the Elliott machine was used.

8. Skin tolerance to diathermy appears still to be the best indicator in preventing damage to the tissues.

9. Gonorrheal and postabortal infections respond more readily than postoperative complications. No attempt was made to kill the gonococcus in any of our cases in which local protracted high fever therapy was given.

10. Psychic factors must be closely evaluated in women complaining of pelvic discomfort.

11. Noteworthy features of conventional diathermy are ease of treatment, local as contrasted with a generalized heating, much more comfort for the patient, relief from pain, decrease in size of inflammatory exudate, less chance of damage to

tissues, fewer treatments necessary and possibility of fertilization at a later date as contrasted with the usual operative barrenness when surgery is resorted to.

CAUTION

The federal law requires all persons using short wave diathermy apparatus to register their equipment with the local authorities. This is a war measure.

384 Post Street.

PNEUMONIA CAUSED BY MICROCOCCUS TETRAGENUS

WALTER R. TOBIN, M.D., CHICAGO

The organism Micrococcus tetragenus was first described by Koch [1] and Gaffky [2] in 1881. It is commonly found in long standing pyogenic processes in association with a variety of other organisms and in this connection is thought to be a secondary invader and a saprophyte. It has also been reported frequently as a primary cause of infection in various parts of the body, such as meningitis, otitis media, postpartum infections, acute endocarditis, septicemia and arthritis. A search of the literature, however, failed to find this organism attributed to the cause of pneumonia except in 3 instances, all of which were reported in foreign literature. The following is a brief summary of these cases:

Delearde [3] in 1897 reported in detail a case of bronchopneumonia due to M. tetragenus in a man aged 49. He recovered the organism in great abundance in practically pure culture. He made note that the disease was severe and characterized by repeated chills. The patient survived but remained in the hospital for six weeks. Castaigne [4] in that year also identified M. tetragenus in a case of pleurisy with effusion, but no mention was made of pneumonia.

Bosc [5] in 1900 reported a case of suppurative bronchitis and bronchopneumonia in a 21 year old patient with autopsy findings. M. tetragenus was recovered from the bronchial secretions in pure culture. This patient also had enterocolitis and suppurative peritonitis at the time of death, and these processes also yielded pure cultures of this organism. Detailed description with illustrations are given embracing the gross and microscopic as well as the bacteriologic aspects.

Byers and Houston [6] in 1913 described a case of severe bronchopneumonia in a 10 year old child that followed in the wake of a comparatively mild infection of the middle ear and upper respiratory tract. Cultures made from the sputum, pharynx, ear discharge and urine were of a mixed variety, but in each case colonies of M. tetragenus were found. M. tetragenus grew from the blood in pure culture. They concluded that this organism was the cause of the pneumonia and not others that were found in the sputum, because the patient's blood gave a high opsonic index to this organism and not to the others, as compared to normal blood serum; also because an autogenous vaccine prepared from the cultures of this organism injected subcutaneously gave a pronounced reaction even in small doses and had a decidedly favorable effect on the clinical course of the disease, whereas a stock vaccine previously administered gave neither reaction nor therapeutic response.

The case presented here was considered worth reporting because the organism was isolated from the sputum, blood and urine early in the disease in pure culture, and because the disease was otherwise uncomplicated.

From the Department of Northwestern University Medical School.
The case reported here was referred to the author by Dr. Stanislaus Novak.

1. Koch, Robert: Zur Untersuchung von pathogenen Organismen, Mitt. a. d. k. Gsndhtsamte **1**: 1-48, 1881.
2. Gaffky, Georg: Experimentell erzeugte Septicämie mit rücksicht auf progressive Virulenz und accomodative Zuchtung, Mitt. a. d. k. Gsndhtsamte **1**: 80-133, 1881.
3. Delearde, A.: Bronchopneumonie à tetragènes purs, Gaz. heb. de méd. et chir. **54**: 637, 1897.
4. Castaigne, J.: Pleuresie purulente et septicémie mortelle produites par la tetragène, Bull. Soc. anat. de Paris **11**: 394-400, 1897.
5. Bosc, F. J.: Contribution a l'etude des infections produites chez l'homme par le micrococcus tetragenus septicus, Arch. de méd. exper. **12**: 159-181, 1900.
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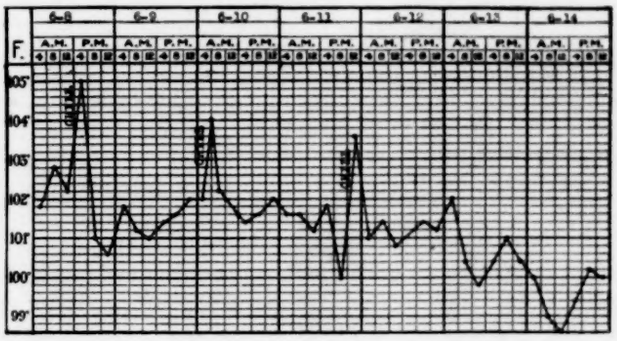
REPORT OF CASE

Mrs. S. M., aged 43, a housewife, had a mild chest cold for about a week and on May 28, 1941 entered the hospital with symptoms of chills, fever, pain in the chest and vomiting. Her temperature was 103.4 F., pulse 126 and respiratory rate 40 to 46 per minute. The white blood count was 13,450 with 96 per cent polymorphonuclear neutrophils. The red cell count was 3,370,000 and the hemoglobin 11 Gm. per hundred cubic centimeters. She appeared very ill and was mildly cyanotic. No definite consolidation was found, but the breath sounds were impaired. Moist rales were heard scattered over the lower half of both lungs, anteriorly and posteriorly. A diagnosis of bronchopneumonia was made and confirmed with x-ray examination. After several unsuccessful attempts to obtain sputum for analysis, a specimen was recovered by means of a tracheal catheter. The cytologic examination of the sputum thus obtained revealed only cocci, few in number, which were not characteristic of pneumococci and did not show capsular swelling by the Neufeld method. Culture of this specimen resulted in the abundant, almost pure, growth of an organism which proved to be Micrococcus tetragenus. A blood culture, taken on entrance to the hospital, revealed the same organism. A few days later the patient complained of frequency and burning of urination, and examination of the urine showed 50 to 100 pus cells per high power field. A pure culture of M. tetragenus was also made from a catheterized specimen of urine. In order to confirm our contention that M. tetragenus was the responsible organism, repeat cultures of the blood, urine and sputum were made and in all 3 instances the results were



Temperature during the second week of the disease, showing malaria-like record.

identical. The sputum was examined for acid fast bacilli, but none were found. The blood Wassermann and Kahn reactions were negative.

The course of the illness was stormy, characterized by repeated chills every one to three days, which were followed by an increase of fever, up to 103 or 104 F. Sulfapyridine was administered by mouth in doses varying from 1 to 2 Gm. every four hours, which maintained the blood level at 9.5 to 11.5 mg. per hundred cubic centimeters. The drug, as is reflected in the temperature curve, appeared to have little effect on the course of the disease. For one forty-eight hour period sulfathiazole was substituted for the sulfapyridine without obvious clinical change in the patient. Potassium iodide was administered by mouth for its supposed effect in disintegrating the capsule, but without effect. Other standard therapeutic measures used consisted of oxygen, frequent blood transfusions, adequate caloric intake, sedatives and the maintenance of water, electrolyte and vitamin balance. Vaccine therapy was not tried. Recovery was gradual, and the patient was discharged from the hospital June 22, twenty-five days after entrance.

SUMMARY AND CONCLUSIONS

A case of bronchopneumonia complicated by bacteremia and urologic infection was due to Micrococcus tetragenus. Sulfonamide derivatives in this case failed to produce a therapeutic response. In view of Byers and Houston's report of successful treatment of a similar case with an autogenous vaccine it would seem advisable to give this method a trial when other readily available measures have failed.

6 North Michigan Avenue.

Special Article

HANDBOOK OF NUTRITION: XX

FEEDING THE AGED

EDWARD L. TUOHY, M.D.
DULUTH, MINN.

These special articles on foods and nutrition have been prepared under the auspices of the Council on Foods and Nutrition. The opinions expressed are those of the authors and do not necessarily reflect the opinion of the Council. These articles will be published later as a Handbook of Nutrition.—ED.

At the outset I present five reasons why practicing physicians should become interested in the problem of feeding the aged. When they convince themselves that overindulgence and needless restriction in food are both wrong, then will their patients gradually conform. They always have conformed and on many occasions have accepted guidance far less scientifically sound than that outlined in this series on nutrition.

1. Those living over 60 are now so numerous that their individual needs call for an active aggressive medical approach. The individual, instead of his disease, is our problem. We must become guides or umpires rather than healers and on a long term, rather than a temporary, basis.[1] The treatment of diabetes with balanced diets and insulin, of pernicious anemia with liver extracts, illustrates the technic. We have asked repeatedly that we be allowed to keep the "physician-patient" relationship. Here is our opportunity.

2. Mass efforts (for preventable diseases) and specifics (for certain infections) have nearly eliminated many common diseases (diphtheria, typhoid). We are on the way to control pneumonia if seen early. Less young people die; more attain advanced age unhampered by a holdover of morbidity from earlier nonfatal encounters that nevertheless leave their scars.

3. The competence of healthy older people is largely a matter of nutrition. Doctors also have an age problem. They also age. America is at war. There is no turning back. Physicians attain their fourth decade before they become active in their respective fields. They need more years of activity after 60 than most are favored with. Coronary disease is all too common with doctors. I shall refer to it at some length because food excesses (fat) may be a factor involved.

4. Population is an asset. Human beings must never be classed as liabilities. Guiding the aging may be made a stimulating medical field. It is not a "second childhood" affair, as the uninformed facetiously imply. Geriatrics is less a science than an art. It is not an isolated specialty comparable to pediatrics. The pediatrician tells the mother or nurse what to feed the child. If the food is available, the child usually gets it. The geriatrician (I do not aspire to be one) usually finds his older subjects neither acquiescent nor especially cooperative. Food habits have become fixed; those under or over eating enjoy their self determination. Accordingly it is not sufficient to tell off average menus suitable for the old. This simple assignment I leave to the scores of available diet manuals. Some argument must be presented to give the whys and wherefores of the need of balance in various foodstuffs and vitamins. The overrefinement of starch and excessive use of sugar must be warned against and the reasons made clear enough so that appetite is not the sole guide to eating. All specialists and general practitioners giving service to the old should familiarize themselves with the researches in nutrition now contributing so effectively where understood and applied.

I shall attempt to assemble the evidence establishing adequate nutrition as the present day primary need of the older age group. The previous chapters in this series have authoritatively outlined the increment in knowledge of nutrition that has come since the turn of the century. McLester in the introductory chapter expressed the fear that, despite all these advances, there may follow an undue lag before this nutritive beneficence becomes a part of our life and heritage. It rests with practicing physicians to limit this lag, to bring about within as few decades as possible (especially for the older age group) something comparable to the improvement in nutrition that has already come to two generations of babies since pediatricians have put the balanced nutrition into effect.

5. We have the present war emergency. There is much salvage within the old age group. No portion of the present nutritional program should be denied the aged on any basis dictated by their years. Age is hard to define. It is known best by what it does. It limits outlook and capacity; it adds its "aches and qualms," all too readily attributed to ingested food. The food left out may contain the elements that complete the vicious circle, so that less food, more infirmity, more symptoms, less efficiency pile up. Age conceals a vast reservoir of talent, skills, wisdom and experience, not to mention much muscle and brawn if proper food maintains reserve. There could not be a better time to plan a purposeful nutritional program for the peace that must follow war. Doctors must take part in it.

This is a machine war—the product of a machine age. In our depression years unemployment, broken homes, improvident children, unpractical subsistence relief or pensions, robbed the old of employment, position, honor and a place in the community. With such crying need for all possible man and woman power it is now or never for us to give back to this group some of what they have lost.

LIFE EXTENSION; FOOD AVAILABILITY; EMPLOYMENT

Life extension has brought great social and economic problems (table 1). I shall add but few of the figures now so freely quoted. The most striking prediction concerns that "22,000,000 people in the United States over 65 years of age" within another generation. Up to the time of our engagement in the war efforts and for ten previous depression years, youth was held back from production. Those discharged over 50 found industry hesitant to reemploy them. Now we face a condition where retirement after 65 promises less and less as taxes and living costs mount, as investment possibilities narrow and pensioners multiply. In the offing there is always the specter of inflation. At present few people think of leisure or retirement; it is timely to

From the Department of Internal Medicine, the Duluth Clinic.

1. Causes of Death, Statistical Department, Metropolitan Life Insurance Company, 1940: Of children born:

	1900	1940
Acute deaths	1 of 3	1 of 6
Chronic disorders	2 of 4	3 of 4

"The only chronic malady showing striking decrease is tuberculosis."

emphasize the great advantage of cultivating health, mental poise and technical skills and avoiding obsolescence. Since the turn of this century the life expectancy of white babies has been advanced sixteen years for females and fourteen for males. This totals up to 67.31 for the former and 62.94 for the latter. The immediate and pressing issue is How may these years be made worth while? Food is a basic requirement; the amount and proportion depend on the individual and where and how he lives. It may be said, with few exceptions, that to deny people work is to deny them food. Now, when production is so much in the forefront of our national demands, we must salvage everything possible, and certainly not the least item in this effort is the group concerning which I write. If justice is ever to obtain, the appeal "Give us this day our daily bread" must exclude none. The way to give it is to plan that all able shall work; doles and subsistence are mockeries. This is a peace program with which a war schedule must be implemented. Otherwise we shall still be at war, for with the military peace we shall continue economic war.

THE FALLACY OF FOOD RESTRICTION FOR THE AGED

A stupendous literature dealing with nutrition accumulates. I append references to certain authors where some may wish to know the source material. The resurgence of interest in dietetics has come at the same time with a reviving interest in medical geriatrics. Many [2] have written articles based on the medical needs of the aged. There is a new edition by Thewlis [3] bringing up to date the pioneering of Nascher; a recent handbook by Boas [4] dealing with the treatment of the patient after 50 is well arranged and documented, and considerable attention is paid to diets. Cowdry's [5] compendium from various authors, including physiologists, biochemists and psychologists, is most readable and informative. Some readers will be displeased that so few positive factual statements may be made. People around the world live well on the most varied diets, each satisfactory as decreed by custom and availability. If the reader would like an American menu for elderly people, there are available countless articles where these may be consulted and individual tastes consulted. Some statements might be "factual" if more were known about aging as a process.

For reasons hard to understand, there is the widest belief that the elderly should be abstemious. The few gluttonous and obese have visited this inhibition on the many who are overconscientious and underweight. We should start with the dictum of Piersol and Bortz [6] "To add life to years rather than years to life." That is the basic motive for campaigning for better nutrition for the aging. What we are looking for is not a dragging out of vegetative almshouse existence but the promotion of real efficiency. The human being attains his full bodily development, let us say, by 40, the beginning of his fifth decade. His next decade and a half pits him against the most stressful period of his life: the time in which early rheumatic and other infections mature and cripple; when arterial hazards (coronary disease) add their tragic interruptions; when metabolic perversions (obesity, diabetes and gout) appear—all when his business, his insurance plans, his educational and family responsibilities are at their height. And this is the period when we ask him to prepare himself for the seventh, eighth and ninth decades which present life extension tables plainly tell him are "just around the corner." This is no longer a promise or objective, it is with us here and now and in very formidable proportions. Dominant as heredity is known to be, we may just as well leave it out of the discussion. Each individual must accept the genetic complement fate has assigned him. He must make the most out of what he has. It must be clear that no one may expect the most from the later age decades when no preparation has been made in adjusting habits, cultivating something of a philosophical attitude toward life and its responsibilities and at least looking about among friends and neighbors for object lessons or examples of men and women who are succeeding in various stations and walks of life in arriving at what we call a comfortable and serene old age. Age is feared much more for the restrictions it may impose than the promise of death. The body as well as the mind must be trained to accept aging. The time to acquire the physical and mental deportment with which to get the most out of life in its later decades is in middle age. The neurosurgeon cannot acquire his skill for the successful removal of a brain tumor when the patient with a terrific headache enters his consulting room. The cultivation of proper food habits early in life is too obviously advantageous to call for further discussion or elaboration. We must learn to grow old skilfully as well as gracefully.

Perhaps "the less food for old people" fallacy hinges on the supposition that for them energy for current expenditure is the chief item and therefore carbohydrate and some fat with a minimum of protein suffice. In any case, that is the way many old people exist but do not live. All living creatures are interrelated and follow universal laws in their metabolism and growth. Life and its products are handed back and forth between living creatures (plant and animal). Nature has provided these laws of balance and coordination. Simpler organ-

TABLE 1.—*Age Level Extensions* *

	1900	1937	1940
Average age at death	26.79†	58.65	62.00
Death under 1 year	24%	5%	5.2%
Death over 75	4%	25%	32.1%
Death at 45 or over	24%	79%	86%

* Statistics furnished through Dr. Mario Fischer, Duluth Health Commissioner.

† There was at that time a high death rate from typhoid and tuberculosis, as well as from complications of all the contagious diseases of childhood. In the summer time there was the traditional high death rate from feeding disturbances in children, and pneumonia was prevalent in the winter. Many woodsmen and miners came into Duluth for terminal hospitalization.

2. Tuohy, E. L.: A Proper and Adequate Protein Diet for Elderly People, Minnesota Med. **25:** 313 (May) 1940. Norman, J. F.: Our Aging Population, ibid. **24:** 1066-1071 (Dec.) 1941. Christian, H. A.: Some Limitations in Preventive Medicine, Ann. Int. Med. **12:** 1499-1506 (March) 1939. Dublin, Louis I.: Medical Problems of Old Age, University of Pennsylvania, Bicentennial Conference Bulletin, Metropolitan Life Insurance Company of New York. Wilder, R. M.: Nutrition in United States: Program for Present Emergency and Future, Ann. Int. Med. **14:** 2189-2198 (June) 1941. McCay, C. M.: Diet and Aging, J. Am. Dietet. A. **17:** 540-545 (July) 1941.

3. Thewlis, M. W.: Geriatrics a Special Branch of Medicine, M. Rec. **153:** 433-435 (June 18) 1941; The Care of the Aged (Geriatrics), St. Louis, C. V. Mosby Company, 1941.

4. Boas, Ernest P.: Treatment of the Patient After Fifty, Chicago, Year Book Publishers, 1941.

5. Cowdry, E. V.: Problems of Aging, Baltimore, Williams and Wilkins Company, 1939 (Josiah Macy Jr. Foundation Publications).

6. Piersol, G. M., and Bortz, E. L.: The Aging Process: Medical-Social Problem, Ann. Int. Med. **12:** 964-977 (Jan.) 1939.

isms accept them, but man has varied notions of his own. He chooses primitively with the least cultivated of his tastes. The result is a diet over-rich in refined flours and sugar. He misses the balanced assemblages plant life has integrated and domestic animals have concentrated for him. They do it better than he can plan it. Hence the appeal for natural foods, including animal products. Human growth is not terminated when adult stature is attained. Witness the manner in which the atrophic smooth tongue of addisonian anemia assumes normal size and coating after optimal exhibition of liver. The Lawrences have shown with Geiger counters how rapidly tagged iodine is picked up by the thyroid. Tagged calcium has been located promptly in tooth enamel, long supposed to be fixed, inert and final for the duration of life. Rates of growth vary, but the process endures with life. Repair within the body is a continuous process and in such organs as the liver may be stupendous. Fixed and overspecialized cells (retina) must also be undergoing some change, as is disastrously connoted when the blood supply is even temporarily interrupted. In that sense reproduction of the individual as a unit is limited by age, but, in the cellular domain, active living processes demand nitrogenous equilibrium continuously. The tea and toast schedule for grandma is outmoded. No old person is a walking museum piece—a holdover from last year's crop—and for the same good reason must not be treated like a barnacle on the ship of state.

Stieglitz [7] has used the term gerontology to cover a study of the aging process, in contrast to geriatrics (care of the elderly). The distinction is proper. Simms [8] has studied Dublin's insurance mortality records and computes that our young adolescent at age 10 is the healthiest human being: only one in eight hundred dies at that age. He states that if such a mortality were maintained the life span would stretch out to 550 years! Age, as a name for what Shakespeare meant, when he wrote "We ripe and ripe and ripe; and then we rot and rot and rot," while indeed baffling to scientists, is very obvious to women of fashion. They are most familiar with what age does to the skin. Roger Bacon thought age concerned the withdrawal of water from the body and was in the nature of wilting. He was well informed; fluid balance connotes integrity. To the three great reserve organs of the body—the liver, the muscles and the skin (commonly listed)—I would presume to add the osseous system, not only for its calcium reserves, but for the housing of the important areas of hematopoiesis. Cannon ventures a practical explanation of age without entering into the chemist's discussion on collagen metamorphoses; he says age witnesses a gradual limitation of homeostasis wherein such body constants as acid-base equilibrium, body temperature, mineral and water balance are still maintained but within progressively narrowed limits. Physiologists strive to produce in animals counterparts of the human diseases they are studying. I was surprised in my reading to learn that not a little research has been done with the lower animals on the problem of age. Simms [8] has made a plea for much greater financial support for research along the lines of determining how age limits physiologic responses. This is directly in line with Stieglitz's [7] gerontology. Simms has developed a method of sublethal bleeding of standardized rats of various ages. The older rats stood the shock (Cannon-Blalock) of this bleeding with "a probability of death sixteen times greater than with the younger rats." Dearing,[9] experimenting with digitalis and its toxic effect on the heart, brain and coronary blood flow, found that his older animals did not withstand the drug nearly as well as the younger. One turns from these laboratory experiments to the obvious deductions of the sports writers. The prize fighter is out by age 30, the baseball player by 35, and now we are told that, to meet the demands of the "blackout" incidental to dive bombing, only the youngest aviators are able to withstand this rigorous test. Fulton [10] has written on the "acceleration factor," the mechanical process by which the swerving plane drives the blood centrifugally so that the flow does not accommodate rapidly enough to the change of direction of flight so that blood attains the higher centers. So the youngest and sturdiest are chosen to sustain these enormous stresses because they better retain consciousness.[11] Youth is able to establish records in the shorter sprints and hurdles, but when prolonged effort is displayed (distance runners, sand hog workers) older men have an advantage accruing from skill and husbanding their strength. Industrialists should remember this. Freeman [12] and others, studying shock, stress the factors of exposure, cold, fatigue, blood loss and water loss. Shock is, in part, an exaggeration of situations beginning as discomforts and mounting to dire upsets of homeostasis and challenging the integrity of the individual by dissociating the orderly functioning of system organs. Elderly people have simpler names for chills, fatigue and exhaustion. Food and drink exhilarate as does nothing else. Add sleep and you have recuperation. Periodic starvation has no place in the care and conditioning of the old and is one of many useless middle age fads. This is the background for practical suggestions I shall make in terms of when and what to eat.

FOOD AND THE CARDIOVASCULAR SYSTEM

"A man is as old as his arteries." This statement has been too long accepted by clinicians. We look at an older person and then palpate the peripheral arteries. "Peripheral vascular disease" is a category that covers many difficulties experienced by the aged. Certain chapters in Cowdry's book discuss a dissociation of aging and arteriosclerosis—the former a natural process beginning before birth, the latter an unnatural acquisition so common that many think it universal. We face a medical problem when many in the prime of life die with 1 centimeter or less of thrombus in the branch of an atheromatous coronary artery, while many octogenarians are hale and hearty with most of their larger arteries laid down in concrete. Wherein does the question of diet enter into this discussion? Is aging hastened

7. Stieglitz, Edward J.: The Urgency of Gerontology, News Edition, Am. Chem. Soc. **19**: 1147 (Oct. 25) 1941; The Potentialities of Preventive Geriatrics, New England J. Med. **225**: 247-254, 1941; Aging as an Industrial Problem, J. A. M. A. **116**: 1183-1187 (March 29) 1941.

8. Simms, Henry S.: The Problems of Aging and of Vascular Disease, Science **95**: 183-186 (Feb. 20) 1942.

9. Dearing, W. H.: The Effect of Digitalis on the Heart, Brain, Electrocardiogram and the Coronary Blood Flow in Experimental Animals, read before the Minnesota Society for the Study of the Heart and Circulation, Rochester, Minn., Nov. 29, 1941.

10. Fulton, J. F.: Physiology and High Altitude Flying, with Particular Reference to Air Embolism and the Effect of Acceleration, Science **95**: 207-212 (Feb. 27) 1942.

11. According to Fulton's article, the luftwaffe has found that its youngest recruits better withstand the blackout if they have been fed large portions of beefsteak.

12. Freeman, N. E.; Freedman, H., and Miller, C. C.: Production of Shock by Prolonged Continuous Injection of Adrenalin in Unanesthetized Dogs, Am. J. Physiol. **131**: 545-553 (Jan.) 1941.

by overeating? Does abstemiousness promise a long life? The answers to these and many similar questions are not forthcoming, but the statement by Simms that many useful years may yet be added through life extension when science discovers how to prove the aforementioned dissociations and produce specific inhibitors points the way. In the meantime we may learn something by looking about us; and, while clinical observations may be loose and indefinite, Spies has significantly commented that our knowledge of the avitaminoses has been substantially advanced by such observations and by testing out the newer pharmaceutic vitamins and ordering better foods.

There is also considerable difference of opinion as to just how much over or under nutrition exists in our country, in different states and among different classes of people. Chapter XXII (Stiebeling) will discuss that issue based on her extensive observations and studies in association with the United States Department of Agriculture.[13] I think undernutrition produces more physiologic disturbances, but overnutrition (fat) may hasten the development of more pathologic change.

Living in a rich agricultural state, I do not see very many people needlessly undernourished. By proper planning and marketing and with attention to the methods discussed in chapter XVI (Cowgill) most of the borderline or marginal degrees of undernutrition which we uncover are economically unnecessary and stem from social maladjustment, anxiety states and outmoded medical advice. Undernutrition reduces vitality and well-being much more than it hastens decline or senility. It is hard to believe that "optimum nutrition" could endanger anybody's vascular system. The trouble lies in finding an "optimum diet"—because it varies with every locale, every people, employment and individual purpose; and nature has distributed around the world the widest assortment of adequate food sources. Some may like a "short life and a merry one"—at least at middle age that is their choice. Whatever the process by which it is brought about, 70 per cent of our Duluth Clinic [14] patients are dying of cancer and cardiovascular-renal disease (including cerebral hemorrhage). This figure for cancer (18 per cent) is higher than the Minnesota State Board of Health figures (14 per cent) for 1941 and represents a higher than average of older people in our clientele. The approximate 50 per cent of cardiovascular renal disease [15] is the same as Simms's claim for all deaths over age 10. I have checked these figures from four old line life insurance companies, and I present in table 2 the results from one of them. The others are almost identical. This detail of end results tells little, of course, relative to incapacity and sickness among the group I am discussing. From many studies dealing with the prognosis in degenerative heart disease it would be fair to state that there is an average illness (partial or complete) of about two years. During that time diet is a part of the treatment and is subordinated thereto. Unless some newer food components (biotin) can be proved to be carcinogenic, preventive measures (diet) in terms of about three fourths of our deaths are very much in that current state of "too little and too late." Table 3 shows clearly enough that the life line of our people is rather well extended. It prompts me to add "I should tell them how to eat and how to spare their arteries!"

13. This department publishes a long list of studies full of interest and information.

14. This study is part of a sampling of our records, with especial reference to the deaths. For the year 1940 and 1941, 1,339 deaths have been carefully traced, covering patients of all ages whom we have seen since 1915.

15. This is the group in which gerontologic research may be most productive (Simms).

THE SOCIAL AND ESTHETIC ASPECTS OF EATING

No discussion on the subject of diets for the elderly should leave out some tribute to food based on values other than its caloric content. Religious, national and family feastings on holidays have been such a civilizing influence that any campaign for better nutrition must never overlook the spiritual and social resources arising from the table or the sharing of food. While vacillating between the dangers of undereating and overeating (a fair optimum diet) I must not appear to condone the gourmand. Women are much more susceptible to food faddisms than men, and fashion is apt to dictate the basis on which many digestive neuroses develop. Dorothy Dix avers, apropos of woman's destiny, "They seem either to become skeletons or feather pillows." It is either a "feast or a famine" with all too many people. Prentice shows that that is history

TABLE 2.—*Causes of Death* *

	Year		
	1941	1931	1921
Circulatory diseases (heart disease, apoplexy and so on)	48.2%	32.8%	25.4%
Cancer and other malignant tumors	10.1	10.2	10.6
Violent deaths (automobile, suicide, aviation)	9.4	16.9	14.1
Respiratory diseases (tuberculosis, pneumonia, influenza)	8.6	14.6	19.3
Digestive and genitourinary diseases (diabetes, nephritis, ulcer, liver)	7.6	12.2	15.9

* From Provident Mutual Life Insurance Company.

TABLE 3.—*Cardiovascular Deaths in Minnesota for 1940*

Total for such deaths	7,693	
Rate per 100,000	275.5	
60 years and over	79.8%	
80 years and over	24.7%	
Death certified from:		
Myocardial disease	28.4%	64.0%
Coronary disease	35.6%	

repeating itself. Hunger is a natural instinct with the young; it is often a luxury with the old. Food must be made attractive. The atmosphere should be conducive to liveliness and some approximation of what Edwin Markham calls man's primary needs: bread, brotherhood and beauty. We need a modern Brillat-Savarin [16] with ability to popularize the nutritional nuggets today's science provides us in the manner in which he popularized esthetic living and dining.

PRACTICAL GUIDANCE

1. *Protein* (chapter II, Lewis).—The need of protein at all ages is now so well established that little argument need be advanced. A few simple statements for the unconvinced should suffice. Note how the "essentialness" of the amino acids keeps step with the components of B complex and B_1. I wish especially to illustrate the significance of the liver in homeostasis. Goldschmidt, Vars and Ravdin [17] noted the liver pro-

16. Brillat-Savarin, Jean Antheline: The Physiology of Taste (Frank Crowinshield translation from original), New York, Boni and Liveright, 1926.

17. Goldschmidt, S.; Vars, H. M., and Ravdin, I. S.: The Influence of Foodstuffs on the Susceptibility of the Liver to Injury by Chloroform and the Probable Mechanism of Their Action, J. Clin. Investigation, **18**: 277-289 (May) 1939.

tecting faculties of protein in their experiments with dogs poisoned by chloroform. Whipple's [18] thesis that animal protein buffers the liver for blood plasma restoration is being augmented each month by various reports, all supporting the conclusions that protein safeguards the normal liver,[19] even as dextrose (Mann and Bollman) tides over the damaged liver. Philip Brown [20] advises a high protein diet in ulcerative colitis in order to protect the liver. The papers by Patek [21] and Butt and Snell [22] show the trend. Starvation edema is a matter of inadequate protein and liver efficiency. Space permitting, I could illustrate some of the follies of "arthritis," "colitis" and nondescript diets that decried the use of meat. A neglected and abused liver sets the individual toward a toppling over of his homeostasis. We may put down then, as our first duty to the aging, Teach them the importance of protein and how to get their quota, no matter how old they are, 1 Gm. per kilogram of body weight. The pellagrin and the alcoholic addict with tremens prove how dependent the brain [23] is on the liver.

Unfortunately, animal protein is expensive. Preservation and refrigeration add further costs. (Consult chapter XV, Kohman.) Those purveying food are in full accord with the present nutritional program.[24] Utilizing the cheaper cuts of meat and making them palatable is a task for properly advised cooks, taught to develop an American goulash, but with a seasoning suitable to the American palate and without too much fat. (Consult chapter XVI, Cowgill.) We may, if harder put, learn to appreciate soy beans. It is a matter of education. It is distinctly possible to be a well fed vegetarian if milk, butter and eggs and cheese are plentiful and time is no object. Primitive peoples of our own times could teach us how the better to utilize the vitamin rich viscera. The occasional azotemic patient and the gouty, at some stage in their imbalance, should have a low protein intake; nearly every other indication, so much a part of books on diet, is a relic of a period in which attention was paid to the appearance and consistency of food and very little to its mineral, vitamin and chemical content.

2. *Fat* (consult chapter III, Bloor).—This is the food with which excess may well be dangerous, but leaving out what is needed is fatal. Burr [25] has demonstrated the essentialness of certain fatty acids, particularly in terms of growth, milk production in cattle and vitamin B economy. Hansen, working with him, has been able to clear up some very trying instances of eczema and dermatitis in children through feeding of certain selected fatty acids. Fat improves the taste of everything. It is the good cook's delight. For the vigorous, it invites overindulgence; even if it does not "burn in the flame of the carbohydrate" both are very compatible (as the obese well know) and energy is released without the specific dynamic action loss characteristic of protein. Fat spares all reserves, including vitamin B and protein. But when it isn't properly utilized, it clogs up the liver.

Biochemists and physiologists are baffled in attempts to trace fat through the human body and understand its interrelations with other food elements. In contrast, a lay knowledge which coined the phrase "living on the fat of the land" acclaims a great and popular appreciation of fat. The housewife chooses the beef where the muscle is well interlarded with white fat. Her husband chooses brown ties to match the gravy. For heavy work in low temperatures where much energy is expended, fat is the chief resource. Finnish woodsmen in northern Minnesota have shown me how they choose the fattest of salt pork; with amazingly sharp knives they sliced this off and sandwiched slabs of it between the bisected halves of firm, hard loaves of bread. As they took a bite through this sandwich, I was told that some with inadequate teeth used the same sharp knife to sweep the mouth free from the segment without displacing a single whisker! With copious draughts of well sweetened coffee and condensed milk, these men [26] could work prodigiously in subzero weather, feel comfortable and maintain their weight. "How about venison?" I asked. They looked very sad and replied "No good." "Eat big hunks, just like hay." Nature herself augmenting the efforts of the game warden!

The results of Leary's rabbit experiments, in which he fed large amounts of cholesterol, have not been entirely refuted. He did prove that in the rabbit it seeped through the intima. Interest centers in the background of what cholesterol phagocytosed into the subintimal layers of the coronaries may later do in encouraging coronary inadequacy, sclerosis and thrombotic pluggage. Hurxthal,[27] who has given much study to the subject of cholesterol (myxedema and related states), offers no especial support to Leary's theory. From Isidore Snapper [28] comes a lively observation apropos of his recent experience in Japanese invaded China. He agrees with many other Occidental exchange professors who have reported from the Orient that the incidence of hypertensive disease and coronary complications is much less there than with us and implies that we have too much butter and cream at our plates. Snapper made a significant and naive observation to the effect that the very polite Chinese imparted to him the news that we Occidentals exude an unmistakable bovine aroma. Lest this be taken as a facetious implication, a recent report by Crohn and Drosd,[29] dealing with the mechanism whereby garlic taints the breath, showed that it is a matter of absorption and reaches the blood stream via the liver and thence to the lungs. Perhaps certain systems are surfeited with fat, and strawberry gallbladder and stones may not be the greatest insult resulting.

18. Whipple, George H.: Production, Utilization and Significance of Blood Proteins, annual lecture of the Minnesota Pathological Society, Journal-Lancet **59:** 482 (Nov.) 1938.

19. The liver deserves a respect comparable to the fabulous "Uncle Bim"—his resources are ever drained but never exhausted.

20. Brown, Philip W.: Suggestions as to Diet in Certain Gastrointestinal Conditions, University of Minnesota Continuation Course in Dietetics, Feb. 20 to 22, 1941 (page 1 of notes).

21. Patek, A. J., Jr.: Treatment of Alcoholic Cirrhosis of the Liver with High Vitamin Therapy, Proc. Soc. Exper. Biol. & Med. **37:** 329-330 (Nov.) 1937.

22. Butt, H. R., and Snell, A. M.: Recent Trends in Treatment of Cirrhosis of the Liver, Proc. Staff Meet., Mayo Clin. **17:** 250-254 (April 22) 1942.

23. It is estimated that one person in five living beyond 65 will need segregation for mental aberrations.

24. It was announced recently that fifteen leading food dispensing corporations had established a million dollar fund with Karl Compton of the Massachusetts Institute of Technology in charge to make sure that their researches and plans were right.

25. Hansen, A. E., and Burr, G. O.: Proc. Soc. Exper. Biol. & Med. **30:** 1201, 1933.

26. This concentrated diet was really an outpost ration: two men occupy a shack for ten days at a time, then go back to their homes.

27. Hurxthal, L. M., and Simpson, H. N.: Hypothyroidism; Hypercholesterolemia, J. Clin. Endocrinol. **1:** 450-452 (May) 1941.

28. Snapper, Isidore: Chinese Lessons to Western Medicine, Interscience Press, 1941.

29. Crohn, Burrill B., and Drosd, Rudolph: Halitosis, J. A. M. A. **117:** 2242 (Dec. 27) 1941.

Recently, at a large clinical panel discussion, the question was put to Tinsley Harrison "If you had a patient with a family history of coronary disease, especially with thrombosis, would you advise the limitation of fat in the diet?" He answered affirmatively. I agree with him. Patients with gout (attacks precipitated by rich fatty foods) are very liable to coronary sclerosis. Such clinical evidence should not be undervalued, at least until more is known about fat metabolism. It is my opinion that, if 10 per cent of the necessary calories for the inactive elderly person are derived from fat, the bodily needs will be safeguarded. Some criticism of the higher caloric intake now advised for our recruits and practiced by our athletes is heard. There is the immediate effect (weight and mobility of recruits) and the remote effect (habits of eating during forced exercise) incompatible with later sedentary lives.

3. *Carbohydrate, Vitamins and Minerals.*—Under this heading I choose to say little about their obvious virtues. I have tried to weave into this discussion a pattern that implies the great advantage of keeping nature's nutritional formulas intact; by avoiding overrefinement or processing, by getting a balanced ration and all the bodily needs will be contained therein. Age imposes certain deprivations—appetite, digestion, absorption—so that, even when a reasonable diet is consumed, certain deficiencies result. This may well occur even when obesity is present. The mouth (including the tongue, lips and fauces) has become the nutritional barometer. Ivy [30] states that gastric acidity slows up after 20, achlorhydria increases considerably after 40; by 65, 35 per cent of people do not secrete acid [31] after a meal and 28 per cent show no response to histamine. Those losing their teeth (often without good reason, focal infection) frequently go through a period of adjustment to dentures when appetite slumps and subnutrition ensues. Lower plates are rarely secure. Sturdy square jawed people accommodate well to dentures, whereas neurotic and anxious individuals with natively poor bites or narrow receding mandibles find themselves unhappy. The former, with dental plates, say "These store teeth are better than my own." The latter try one dentist and denture after another. The prophylaxis for their dilemma goes back two to five decades. Is diet at fault? Weston Price [32] thinks so. All nutritionists should read his book. He has gathered information from all around the world. The illustrations alone would seem to prove his thesis: native peoples (on the most varied source foods), when they get a balanced food and avoid overrefinement of flours and sugar excesses, bear children with properly formed jaws; the teeth are regularly spaced and both gums and teeth survive. On the contrary, as soon as they move to a region where overrefined carbohydrate in excess is available they promptly lose their teeth. The story is the same whether it concerns the cloistered group in the upper valleys of the Swiss Alps, the Hebrides Islands, African jungle tribes or our Eskimos and Indians. On the other hand, this thesis has so far little support from our leading dental colleges. Irwin [33] has collected a questionnaire from eight teachers holding professorships in basic university departments of medicine and dentistry in the United States. Five questions were posed bearing on caries and pyorrhea alveolaris, resistance thereto, the effect of diets on pregnant women, the babies' teeth, dentition and general development. Opinion or belief that diet was of little import shaded into the belief expressed by a few that nutrition was the basis of all caries and pyorrhea. I believe that this is one of the most pressing nutritional problems before us today. The lack of unanimity I mention is little short of alarming. The dental and medical professions have drifted too far apart. Harvard University's plan to remerge them is opportune.

Twenty per cent of the first draft [34] recruits could not qualify because of inadequate teeth. Surely something is wrong, and the best lead we have involves diets. Bleeding gums are controlled in most people by adequate citrous fruits; so-called trench mouth is an avitaminosis: when tissue dies the Vincent's organisms multiply. The deeper deprivations that come from faulty absorption from the gastrointestinal tract or from diarrheas are pathologic. At the same time we do not know to what extent the age factor produces alterations of absorption and metabolism for which it isn't feasible to get all the essential vitamin and mineral even from a diet that is adequate. There is a good field here for vitamin reinforcement.

Vitamins have not been overemphasized, but the public (at least fifty million dollars' worth of vitamin preparations was sold in the United States last year) and doctors have taken the vitamin detour to supposed nutritional sufficiency and are using various vitamin compounds as they would "bitter tonics." THE JOURNAL (through the Council on Foods and Nutrition and the Council on Industrial Health [35]) has given a clear statement of that fallacy, and it applies in part to the field of my discussion. Among segregated groups of the elderly there is a place for evaluating the benefit of certain selected vitamins, food enforcement with scientific controls. This has been reported on by Stephenson and his co-workers [36] in England. There was an advantage of such enforcement. I have found many situations and reported on a few in which such utilization in the old induced a health transformation.

Closely related to the tooth problem is that of calcium and phosphorus ratios in the body. Among the elderly (women more than men) senile osteoporosis frequently is found. Albright, Smith and Richardson [37] have linked this up with an endocrine (internal vitamin) estrogenic deficiency. Gardner and Black have reported less dense bone shadow (x-rays) in many nervous and underfed individuals with irritable colons. Hip fractures are common and often fatal; telescoping of the vertebra (with root pains and confusion with angina) occurs after insignificant trauma. By whatever method we try to recalcify such bones, the results are discouraging. I stress this to question the use of milk as a source of calcium for old people. They do not need the fat in whole milk; skim milk is constipating if

30. Ivy, cited by Cowdry.[5]

31. Achlorhydria predisposes to decalcification, enteritis, diarrhea and general deficiencies.

32. Price, Weston A.: Nutrition and Physical Degeneration, New York, Paul B. Hoeber, Inc., 1939.

33. Irwin, Vern D.: Nutrition and the Teeth, Northwest Dentistry **20:** 201 (Oct.) 1941.

34. Among our families in the highest income bracket, many young girls need orthodontic adjustment of their teeth and jaws. Teeth thus pulled by braces are, in my experience, apt to be short lived.

35. Indiscriminate Administration of Vitamins to Workers in Industry, Council on Foods and Nutrition and the Council on Industrial Health, J. A. M. A. **118:** 618-621 (Feb. 21) 1942.

36. Stephenson, W.; Penton, C., and Korenchevsky, V.: Some Effects of Vitamins B and C on Senile Patients, Brit. M. J. **2:** 839-844 (Dec. 13) 1941.

37. Albright, Fuller; Smith, Patricia H., and Richardson, Anna M.: Postmenopausal Osteoporosis; Its Clinical Features, J. A. M. A. **116:** 2465-2474 (May 31) 1941.

taken in large amounts and bulky foods promoting residues are left out. Cheese, buffered with vegetables, is more practical.

Water is too often neglected. Coffee and tea are preferable to chocolate, and, aside from encouraging insomnia, few suffer from their abuse. When not too strong, even in advanced years, these help greatly to keep up fluid intake. They are too often left out on rather poor excuses.

OPERATIONS AFTER SIXTY-FIVE

Surgery for the elderly (cancer, gastrointestinal, genitourinary and central nervous system) is a test that many elderly must meet. Few prepare for it. Emergencies shorten the period of possible preparation. The medical attendant has a heavy responsibility which the surgeon should share with him. At the same time necessary surgery must not be withheld, because many of the elderly do astonishingly well even when the severest operations are done.

Wilcox and Clagett,[38] reporting from the general surgical sections of the Mayo Clinic for 1939 and 1940, listed 1,204 such patients over 65 operated on. The mortality was not high (8 per cent) for benign disease and operable cancer and 16 per cent for inoperable cancer and palliative operations. However, only 20 per cent (one in five) failed to have some significant postoperative complication. Naturally these were in the nature of cardiovascular insults (thrombophlebitis, embolism, pulmonary atelectasis and cerebral and kidney complications). This is what we all see within this group. What better preparation could they have had than even a fair nutritional balance? Added incentive to "keep your body as fit as you can as long as you can" arises from the great likelihood that some major operation or infection is in the offing. These operations are part of the price we shall pay for both the fuller and the longer life.

GENERAL SUMMARY OF DIETARY SUGGESTIONS FOR THE OLD

1. Elderly people should start the day with a good breakfast. It should include some substantial protein, and whatever else depends on body weight and activity. Protein adequacy must be maintained at all ages.

2. As effort lessens and sedentary life supervenes, weight rise or fall should dictate the proportion of carbohydrate taken, and as much of this as possible should be from whole grain. While bran is objectionable cracked wheat products are not. Enriching flour may be a good expedient but the objection to dark breads should be lived down. Potato is the next best starch.

3. For the obese, vegetables and fruits should act as the "fillers" and provide appetite and zest for eating by meticulous preparation and serving.

4. The elderly should eat fat sparingly, even as the middle aged should use it cautiously. The high cholesterol sources (egg yolk, cream and animal fats) should probably be curtailed wherever body build, family history and other indications portend atherosclerosis. It is the one decisive indication for dietary restriction after full stature has been attained. The danger of high blood cholesterol is not universal.

5. Tea, coffee and alcohol are useful stimulants. The abuse of alcohol places it for some people in the category of both refined carbohydrate and animal source fat. As a vasodilator it inspires as well as flushes the aged. One cannot say as much for tobacco. It soothes and cuts off circulation. The quiet postprandial puff is rapidly becoming a continuous process. Tobacco is safer after 60 than before, because age has by that time made the blood vessels less elastic and labile.

6. Food and water (hot drink) taken at regular intervals revive the old. Food becomes the best sleep producer even though early wakefulness follows. Fruit juices add the needed vitamin content.

7. Hunger lessens as age advances. Foods useless calorically (condiments, broth, relishes) have a place. The teeth, gastric acidity, probably absorptive powers, vitamin storage—all begin to fail with age. We are able to compensate for these losses with vitamins, iron, calcium, hydrochloric acid and a balanced diet. The mouth becomes the nutritional barometer of health.

38. Wilcox, L. E., and Clagett, O. T.: Surgical Procedures on Patients of Advanced Age, Proc. Staff Meet., Mayo Clin. **16**: 75 (Dec. 10) 1941.

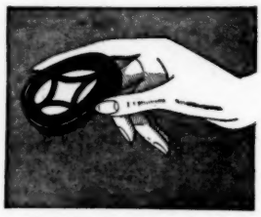
Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING ARTICLE. HOWARD A. CARTER, Secretary.

MAICO HEARING AID, ACE MODEL, ACCEPTABLE

Manufacturer: The Maico Company, Inc., 2632-2636 Nicollet Avenue, Minneapolis.

The Maico Hearing Aid, Ace Model, is a vacuum tube instrument. The dimensions and weights of the various parts are as follows:



Maico Hearing Aid, Ace Model.

Microphone and amplifier unit, ovoid shape, 2¾ by 1¾ by 1 inches, weight 2 1/10 ounces.

A and B batteries in leather case 4½ by 4 by 1 inches, weight 13½ ounces. Crystal receiver, 1 inch diameter by 3/16 inch thick.

BATTERIES

The A battery is a 1.5 volt cell, Maico A No. 728. The current drain is 70 to 80 milliamperes. The B battery is an Eveready 45 volt unit and shows a current drain of 2.30 milliamperes. The two are assembled in a single unit by a well designed connection.

INTERNAL NOISE

With customer fitted ear mold the instrument can be turned to full volume without feedback squeal.

ACOUSTICAL GAIN

The following figures give the order of magnitude of the increase of sound intensity level at the ear of the wearer over that at the microphone under normal conditions of use as shown by audiometric measurements. They are not the same as the electrical amplifications shown by measurement of electrical input and output. Measurements were made only at octave intervals.

Frequency	128-256	512-2,048	4.096
Volume setting full on.....	Nil	24-43	10 decibels

ARTICULATION

The usual syllable and sentence lists were used with hard of hearing subjects at a distance of 5 feet in a quiet room, with instrument set for comfortable hearing. The articulation tests showed satisfactory results.

The Council voted to accept the Maico Hearing Aid, Ace Model, for inclusion in its list of accepted devices.

Council on Pharmacy and Chemistry

REPORTS OF THE COUNCIL

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT.

AUSTIN E. SMITH, M.D., Secretary.

HUMAN CONVALESCENT MEASLES SERUM and HUMAN CONVALESCENT SCARLET FEVER SERUM

HUMAN CONVALESCENT MEASLES SERUM

Measles (morbilli) is an important public health problem because of its universal distribution, the susceptibility of both sexes, and because no age group appears to be exempt, although the majority of the attacks occur in children under 5 years of age. The disease is extremely infectious and may spread rapidly in unprotected communities, there appearing to be little evidence that natural immunity ever occurs.[1] Although the acute manifestations may be extremely mild, the possibility of complications must always be considered, and it is now generally agreed that in many instances children, especially, should be afforded some degree of protection. Other factors requiring special consideration are malnutrition, debilitating diseases and pregnancy. The control of measles from a public health point of view appears to have met with little success[2] and isolation of the sick has not been generally effective in protecting others from the disease.[3] At the present time there appear to be two agents which have shown some success in the prophylaxis and modification of an attack of measles: these are Immune Globulin (Human), which has been accepted by the Council on Pharmacy and Chemistry for inclusion in New and Nonofficial Remedies, and Human Convalescent Measles Serum.

The use of human convalescent measles serum dates back about twenty-five years, and encouraging reports have appeared in many parts of the world. Harries[4] reported that five doses of 10 cc. of recently prepared convalescent serum given intramuscularly would protect an exposed child for a period of about three to four weeks. This investigator could obtain an attenuation of an attack of measles by using lesser amounts or delaying the injection for four to eight days after exposure. Attenuation did not appear to prevent the development of immunity against subsequent attacks. Again, Harries claimed that the serum had no effect when injected after the eighth day following exposure, unless given intravenously. Price[1] states that the intramuscular injection of human convalescent measles serum produces a passive immunity lasting about one month: if the injection is given after the sixth day, the attack will persist but in a modified form which nevertheless results in a lasting active immunity. He suggests an average dose of 5 cc. for a child, the dose being increased as needed, and he believes that all children under three years of age exposed to measles should be given preventative therapy.

Grod[5] studied the use of mixed serum in 170 children and reported the serum was tolerated even on repeated administration. Doses of 15 to 20 cc., usually injected on the fourth or fifth day of incubation, afforded apparently complete protection in 47.7 per cent of 44 children who were closely observed. In 36.3 per cent the severity of the attack appeared to be reduced, and in 16 per cent there was no perceptible effect. According to Grod, the results were about the same as those obtained with placental immune globulin, human, but the serum seemed to be better tolerated. A communication by Timmerman[6] indicated that he obtained partial or complete protection in the majority of 98 Dutch children who were at home and in various institutions. In discussion of the prophylactic work which the physician may undertake, de Ruiter[7] recommends administration of the serum on the fourth or fifth day of incubation to obtain an attenuated attack. Hoyne[2] discussed the use of convalescent serum, and while emphasizing the value of the prevention in hospitals and other institutions, suggested that intramuscular injection of 5 to 10 cc. within three days of the date of exposure would result in protection for three weeks. If an attenuated form of the disease is desired, serum or immune globulin may be employed later in the incubation period, although a warning was issued against employing this procedure in a hospital since the modified disease may still be contagious and susceptible individuals may develop severe attacks. This article also discusses the use of 10 to 30 cc. of serums on patients in the preeruptive stage by Gunn in 1934, the intravenous injection of 5 cc. in children by Kohn, Klein and Schwartz in 1938 with alleviation of the disease in about 85 per cent of the cases, and the work of Connor reported in 1939, giving a total of 50 treated cases. The text of Hoyne's paper was substantiated in the accompanying discussion by one clinician who had used convalescent serum in a number of cases with beneficial results.

In reporting on the use of serum in an outbreak of measles in Wellington in 1938, Champtaloup[8] claimed he has been able to prevent or attenuate the attacks in exposed children and to decrease the time for recovery and the complications. Bull[9] used adult pooled serum in an outbreak of measles in Melbourne, and his observations were in agreement with those of Champtaloup in that the severity of the attacks appeared to be lessened and the evidence of complications decreased. Champtaloup began his injections with a minimum of 5 cc. but later increased this to a minimum of 7 cc.; Bull used 10 to 20 cc. according to the age and condition of the patient. Thalhimer,[10] Lempriere[11] and Loewenberg[12] also have issued favorable reports.

While the evidence on the use of human convalescent measles serum in the treatment of the full blown disease is not impressive, the results from its use for prophylaxis or early modification of measles are favorable in many cases and they appear to be about equal to those resulting from the use of Immune Globulin (Placental Extract). The Council on Pharmacy and Chemistry has declared this serum acceptable for inclusion in New and Nonofficial Remedies and several brands are now described in N. N. R. 1942.

HUMAN CONVALESCENT SCARLET FEVER SERUM

Like measles, scarlet fever (scarlatina) is a disease which is highly infectious and no age group appears to be exempt, although the majority of the attacks occur in the young. Agents for prophylaxis and modification of the course of the disease are scarlet fever streptococcus toxin, scarlet fever streptococcus antitoxin and human convalescent scarlet fever serum. The use of serum for prophylaxis and treatment has been discussed by Hoyne, Levinson and Thalhimer (1935), Hyland and Anderson (1937) and Moore and Thalhimer (1939). The latter authors[13] cited the work of the aforementioned and various other investigators when reporting on the bactericidal substances and antitoxin found in the serum of patients convalescing from scarlet fever. These authors advise pooled specimens for a polyvalent serum. A later communication by Thalhimer[10] discussed dosage and use of serum intravenously as well as intramuscularly, the former route being recommended for the treatment of the disease. Platou, Dwan and Hoyt[14]

1. A Textbook of the Practice of Medicine, edited by F. W. Price, ed. 4, Oxford University Press, 1934.
2. Hoyne, A. L.: Measles in 1938: Analysis of 400 Cases—Twenty-Eight Instances of Encephalitis, Illinois M. J. **76:** 136 (Aug.) 1939.
3. Holroyd, F. J.: The Prevention and Modification of Measles, West Virginia M. J. **35:** 121 (March) 1939.
4. Harries, G. E.: The Treatment of Whooping Cough and Measles, Practitioner **142:** 711 (June) 1939.
5. Grod, H.: Moderne Masernprophylaxe, Med. Welt **13:** 1192 (Aug. 26) 1939.
6. Timmerman, W. A.: Serum from Convalescents in Combating Mortality, Nederl. tijdschr. v. geneesk. **83:** 1346 (March 25) 1939.
7. de Ruiter, H. I.: Prophylaxis of Measles, Nederl. tijdschr. v. geneesk. **83:** 1356 (March 25) 1939.
8. Champtaloup, M. A.: Adult Serum in the Prevention of Measles, New Zealand M. J. **38:** 206 (June) 1939.
9. Bull, H. W.: Pooled Adult Serum in the Prophylaxis of Measles, M. J. Australia **1:** 228 (Feb. 17) 1940.
10. Thalhimer, William: Convalescent Measles and Scarlet Fever Serums, Canad. Pub. Health J. **31:** 51 (Feb.) 1940.
11. Lempriere, L. R.: Adult Serum in a School Epidemic of Measles, Brit. M. J. **1:** 1136 (June 3) 1940.
12. Loewenberg, E.: Etude epidémiologique de la rougeole (modifications subris par l'application de serum de convalescent), J. de méd. de Paris **60:** 12 (Jan. 10) 1940.
13. Moore, Elizabeth, and Thalhimer, William: Immunologic Properties of Scarlatina Convalescent Serum, Am. J. Dis. Child. **58:** 1039 (Nov.) 1939.
14. Platou, E. S.; Dwan, P. F., and Hoyt, R. E.: Streptococcus Convalescent Serums (Scarlatinal): The Potentialities of Type Specific Pools, J. A. M. A. **116:** 11 (Jan. 4) 1941.

have also commented on the value of pooled convalescent serum. Viole [15] claims that any reactions are easily controlled.

Thalhimer,[10] Fox and Hardgrove [16] and Rascoff and Nussbaum [17] have made some comparison between sulfanilamide and human convalescent scarlet fever serum; Thalhimer advises that statistical evidence on the concurrent use of sulfanilamide is lacking, whereas Rascoff and Nussbaum suggest its concurrent use in severe and moderately severe scarlet fever until evidence to the contrary is produced.

Lucchesi and Stein [18] compared the effect of four types of treatment on fever and complications in 1,780 patients; one group was treated symptomatically, another received scarlet fever antitoxin, another group was given foreign protein in the form of diphtheria antitoxin and the fourth group received convalescent serum. The authors concluded that convalescent serum in the doses used (30 to 90 cc.) had no effect on the reduction of the febrile state or of complications. Like Lucchesi and Stein, Toomey [19] is not enthusiastic over the results which follow the use of convalescent serum. However, Schultz [20] practices passive prophylaxis in his clinic chiefly with human serum, and Bejarano,[21] after studying the use of serum in soldiers, concludes that it is of value in the prevention and treatment of scarlet fever.

The Council has recognized the use of this serum for prophylaxis but, since opinion was somewhat divided on its merit in the treatment of scarlet fever, inquiries were addressed to professors of pediatrics and recognized investigators in the field of serum therapy in an effort to obtain a representative judgment. The replies of the authorities consulted are quoted in part:

Dr. Francis G. Blake, New Haven, Conn.: "Ever since 1924 we have found the horse scarlet fever antitoxin so satisfactory, provided adequate dosages are used, we have not had any real experience with human convalescent serum. While it is true that an occasional patient, highly sensitive to horse serum, has been treated with human serum, the number is too small to be of any statistical significance. In my opinion the major, if not the sole, value of human serum depends on its antitoxin content. This is, of course, relatively low compared with horse antitoxin. In severe cases I think it would require anywhere from 300 to 500 cc. of human serum to get the same effect expected from 20,000 to 40,000 units of antitoxin, which is the general range of dosage that we use in patients sick enough to be treated. The criteria for benefit are, first, rapid fading of the rash; second, critical fall of temperature and pulse rate, provided the case is not too far advanced and complicated by sepsis. It is my opinion that the septic aspects of scarlet fever are perhaps now better treated by chemotherapy than by so-called convalescent immunotransfusion."

Dr. Murray B. Gordon, Brooklyn: "In answer to your recent letter with reference to the use of convalescent serum in scarlet fever, I wish to advise you that I do not use it in my private practice or at the Kingston Avenue Hospital. I am enclosing a reprint of some recent work done at the hospital with scarlet fever antitoxin (Gordon, Murray B.; Litvak, Abraham M., and Caronna, Victor: Streptococcic Meningitis and Abscess of the Brain Complicating Scarlet Fever, *Am. J. Dis. Child.* **53**:1447 [June] 1937)."

Dr. Archibald Hoyne, Chicago: "For approximately twenty years we have used human convalescent scarlet fever serum for the treatment of scarlet fever at both Cook County Contagious Disease and at Municipal Contagious Disease hospitals. Originally it was given only to a comparatively few patients who were suffering from severe types of the infection. After the serum center at Michael Reese Hospital was established, the supply of convalescent scarlet fever serum was made available in much greater quantity and its use was extended to an increased number of patients. Since 1931, when the Samuel Deutsch Serum Center was founded, more than 23,025 patients with scarlet fever have been treated at Municipal Contagious Disease Hospital. Approximately one third of that number received scarlet fever convalescent serum, which was administered as a rule only to patients with the most severe types of the disease. Our reasons for believing that this form of therapy is of value are based on the following:

The customary sharp decline in temperature within twelve hours after the administration of serum.

The voluntary statement of patients with regard to their improved well-being the day after serum administration.

The marked improvement in throat symptoms, the rapid fading of the rash and the small number of complications in serum treated patients.

We also give convalescent scarlet fever serum late in the course of scarlet fever regardless of the duration of the disease if the patient has serious complications or is in a critical condition. Moreover, our fatality rates are usually extremely low for hospital patients.

"In my opinion there is little if any difference between the therapeutic results attained with human convalescent scarlet fever serum and scarlet fever antitoxin in the early acute stages of scarlet fever. I feel convinced this is true notwithstanding that convalescent serum may possess far less scarlet fever antitoxin than scarlet fever antitoxin serum.

"For your convenience I am forwarding a reprint relating to this subject which you may care to glance through (Hoyne, Archibald L.; Levinson, Sidney O., and Thalhimer, William: Convalescent Scarlet Fever Serum, The Journal, Sept. 7, 1935, p. 783)."

Dr. P. F. Lucchesi, Philadelphia: "In 1933 we studied a series of 1,780 scarlet fever patients with various types of treatment including convalescent serum and concluded that it is neither practical nor of value in the treatment of scarlet fever.

"I am enclosing a reprint in which the exact number of cases treated by various methods is given (Lucchesi, Pascal F., and Stein, Bernard B.: A Comparison of Therapeutic Agents in the Treatment of Scarlet Fever, *Pennsylvania M. J.* **44**:162 [Nov.] 1940). I am of the opinion that scarlet fever antitoxin is of greater value for the treatment of this disease than convalescent serum, since most of the symptoms and signs in the early stages are due to the absorption of the scarlet fever streptococcic toxin.

"In my experience I have found convalescent serum in the treatment both therapeutically and prophylactically helpful in only one disease; that is, measles."

Dr. Edwin H. Place, Boston: "I can say with complete definiteness that convalescent scarlet fever serum has a striking effect on the toxemia of the disease practically without exception. The effects produced are the relief of fever, central nervous system effects when present, and disappearance of the exanthem and enanthem. In about 50 per cent of the cases there is relief of the more obvious bacterial damages and, although this may be due to antibacterial bodies, I am strongly inclined to believe this is a secondary effect from neutralization of the toxin. These opinions are based on several thousand cases with concomitant controls over the past twenty years.

"We have not been able to find any better results from scarlatinal (horse) antitoxin. For several years we have used almost wholly the convalescent serum instead of horse serum antitoxin, as the antitoxin has been associated with frequent and at times severe serum disease. The state laboratory has not yet been able to produce a serum as free from after effects as that for diphtheria. The Lederle serum, and from Toomey's results Parke-Davis serum, are extremely satisfactory but no better than the convalescent serum."

Dr. John Toomey, Cleveland: "Human scarlet fever convalescent serum has a place in the treatment of toxic individuals who are allergic.

"Treatment involves a consideration of many factors, the first of which is who should be treated by specific therapy, either human or animal. The mortality rate from scarlet fever is extremely low (almost negligible), and the majority (nearly

15. Viole, Pierre: Use of Human Convalescent Scarlet Fever Serum in Streptococcic Infections Involving Ear, Nose and Throat, Ann. Otol., Rhin. & Laryng. **49**: 639 (Sept.) 1940.

16. Fox, Max, and Hardgrove, Maurice: Scarlet Fever Therapy: Comparison of Convalescent Serum and Sulfanilamide, Am. J. M. Sc. **199**: 495 (April) 1940.

17. Rascoff, Henry, and Nussbaum, Sydney: Therapeutic Procedure for Scarlet Fever: Comparative Studies, Am. J. Dis. Child. **60**: 552 (Sept.) 1940.

18. Lucchesi, P. F., and Stein, B. B.: Comparison of Therapeutic Agents in Treatment of Scarlet Fever, Pennsylvania M. J. **44**: 162 (Nov.) 1940.

19. Toomey, J. A.: The Management of Scarlet Fever and Its Complications, Pennsylvania M. J. **43**: 769 (March) 1940.

20. Schultz, W.: Prophylaxis of Scarlet Fever, Deutsche med. Wchnschr. **66**: 396 (April 12) 1940.

21. Bejarano, J. F. R.: Empleo del suero de convalesciente de escarlatina en el Ejercito Argentino, Prensa med. Argentina **27**: 306 (Feb. 7) 1940.

90 per cent) of those who die do so not from toxicity but from sepsis, long after plenty of antitoxin has been formed in the blood stream. Therefore it would seem that specific therapy of any kind should be used only where clinically there is a marked amount of toxicity, and only at the start of the disease.

"When antitoxin was first brought out by the Dicks, we used some of the first lot of antitoxin they made but stopped after treating 14 cases. We lost 3 patients after intravenous injections of this material with protein shock ending in pulmonary edema, the symptoms starting about twenty minutes after the antitoxin was given. We refused to use antitoxin further and from 1925 to 1931 used convalescent scarlet fever serum in hundreds, in fact a few thousand cases—the exact number I haven't at hand. However, we know that the temperature does drop when a pooled yield of human serum is used and, it is my impression, although I haven't proved this, that the complications were lessened.

"Several years ago the old scarlet fever antitoxin was concentrated and, instead of using 20 cc. as was once the dose, one could use the newer material concentrated from 20 cc. to 3 cc., the albumin fraction having been removed (Lederle and Parke, Davis & Co.). We had so few reactions and the response was so uniform that we saw no further need to use human convalescent serum in the majority of instances because we now had a standard product which could be checked and which did not vary. The results are on record, and they are excellent. Since we have reported these, we have used it (Lederle Laboratories, Inc., and Parke, Davis & Co.) in over a thousand more cases and have no reason to change our mind; in fact, we feel that the complication rate has definitely decreased. This latter is difficult to estimate, however, because as you know we have the added factor of sulfonamide therapy to consider. In 1936 and 1937 we had 13 cases of streptococcic meningitis with one recovery, and in 1938 and 1939 12 cases, all of which recovered. Thus the effects of the dye on complications has to be remembered in the general picture.

"It is our impression, however, that there has been a definite decrease in complications with the use of specific serums where sulfonamides have been used. Our practice is to use sulfonamides late, not early, because we have found them to be of no value in toxic conditions.

"It is my opinion that human convalescent serum does have a place in treatment of allergic types of individuals, although I will admit that the existence of these cases is more apparent than real. We have not found it necessary to use human convalescent serum except in 2 instances in the past two years."

Dr. Franklin Top, Detroit: "I am enclosing two reprints which serve to summarize the experience of this service with respect to treatment of moderately severe scarlet fever, not only with convalescent serum, but comparing its use with scarlet fever antitoxin and a control serum consisting of 1,000 units of diphtheria antitoxin. In a subsequent study reported in THE JOURNAL OF THE AMERICAL MEDICAL ASSOCIATION, convalescent serum was compared with scarlet fever antitoxin and sulfanilamide in alternating cases of moderately severe scarlet fever. Definite criteria of evaluation were set up for both studies, and the results are given in the papers. (The reprints sent are Top, F. H., and Young, D. C.: Specific and Nonspecific Serum Treatment of Scarlet Fever, *Am. J. Pub. Health* **29**:443 [May] 1939. Top, F. H., and Watson, E. H.: Reduction of Serum Reactions, *Am. J. Dis. Child.* **62**:548 [Sept.] 1941. Top, F. H., and Young, D. C.: The Treatment of Moderately Severe Scarlet Fever, THE JOURNAL, Dec. 13, 1941, p. 2056).

"Briefly, 30 cc. of convalescent serum given intramuscularly appears to be as good as a therapeutic dose (6,000 units) of scarlet fever antitoxin, and both appear to be slightly better than sulfanilamide given by mouth in a dose approximating roughly ¾ to 1 grain per pound of body weight daily for an average of six and a half days during the acute stage.

"In the first study it was apparent that the use of a nonspecific (1,000 units of diphtheria antitoxin) made a marked difference, and the effects, with respect to the number and proportion of cases which needed augmented treatment, on the temperature pattern, number of complications and dismissal status are noted.

"We have also used convalescent serum by the intravenous route in doses of 30 to 100 cc. in borderline septic cases and in some instances of moderately severe scarlet fever. Used by this route, effects are often dramatic; as much so as the use of scarlet fever antitoxin intravenously in cases of toxic scarlet fever.

"I believe that convalescent serum, when available, is of distinct value because therapeutic effects are obtained without sensitizing a person to horse serum which follows the use of the scarlet fever antitoxin. I realize that during the past several years antitoxins have been despeciated to such an extent that serum reactions are much less frequent, but serum sensitization still occurs. When available, therefore, I prefer to use scarlet fever convalescent serum for the moderate or moderately severe case. It is wholly inadequate in the treatment of the septic or toxic types."

Dr. Bernard B. Stein, Philadelphia: "In my experience of eight years as chief resident physician of Philadelphia Hospital for Contagious Diseases, where I saw and treated upward of 100,000 cases of scarlet fever, I believe the pooled scarlet fever convalescent serum has a definite place in treatment—in the patient who is very septic or toxic and is extremely allergic to antitoxin (horse serum)."

Dr. Conrad Wesselhoeft, Boston: "The efficacy of human convalescent scarlet fever serum in the early treatment of scarlet fever was established prior to the introduction of the Dick antitoxin. I have in mind a composite chart to that effect shown at several meetings by Dr. Edwin H. Place of the Boston City Hospital. Since the introduction of the Dick antitoxin, and even since its great improvement whereby serum sickness has been greatly reduced, pooled convalescent serum has a distinct place in the therapy of scarlet fever.

"From a purely theoretical point of view, the attitude that because convalescent serum is not standardized it is always inferior to standardized antitoxin is not in keeping with the limitations of our present knowledge of the disease. Furthermore, it is obvious that a commercial antitoxin, which must be polyvalent to meet the possible needs of different strains, may be lacking in a certain direction quite as much as an unstandardized pooled serum. The advantage of human serum as a means of avoiding serum sickness has been reduced by the refinement of antitoxin, but such refinement has not as yet overcome this advantage.

"Time does not permit me to produce exact figures. Roughly, my experience in scarlet fever covers 20,000 cases at the Haynes Memorial Hospital. The number treated with convalescent serum was increasing up to the introduction of the Dick antitoxin. As the first Dick antitoxin results gave 35 per cent serum sickness, the convalescent serum was again preferred. Three bad Arthus reactions caused us to give up antitoxin entirely. Then as the antitoxin was improved it again came into favor. It would take too much time from my secretarial staff to give you the number of cases in which convalescent serum has been used, but I continue to use it in about one fifth of the cases. As we have had an average of 100 cases of scarlet fever on the daily census for the past six months, it would seem that over this period 120 cases have been given convalescent serum.

"The criteria of benefit are the abrupt drop in the fever and the blanching of the rash. In the past ten years I have rarely lacked such cases to show at clinics. The dramatic results are so well known when the serum is given early and in adequate dosage that I am not inclined to yield my preference for convalescent serum. Such preference is not by any means absolute, as there are situations in which I prefer antitoxin."

In view of the evidence available, the Council recognized this serum as being of value in transferring passive immunity to a patient exposed to scarlet fever. Existing evidence does not appear to indicate that it is wholly adequate in the treatment of septic or toxic types of scarlet fever, but the consensus seems to be that this serum may have a place in the treatment of individuals sensitive to horse serum and where it is desired not to sensitize a person to horse serum. The Council on Pharmacy and Chemistry has declared this serum acceptable for inclusion in New and Nonofficial Remedies, and several brands are now described in N. N. R. 1942.

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SATURDAY, JANUARY 2, 1943

INSULIN RESISTANCE

Many cases in which insulin has failed to lower the blood sugar in the normal manner have been recorded since insulin first came into use in 1922. Glassberg, Somogyi and Taussig [1] observed a diabetic patient who was relatively refractive to insulin for some months and who responded only to enormous doses, as much as 1,100 units in twenty-four hours. The diabetes in this case was due, the authors suggest, not only to a lack of pancreative secretion but also to a lack of some substance which activates insulin, probably a muscle enzyme (phosphatese, insulin complement, glycomutin). Apparently there may exist two types of diabetes: one due to pancreatic disease, which responds to insulin, the other due to a deficiency in the production of a substance which activates insulin. Marble [2] reported observations on a woman with chronic rheumatoid arthritis and diabetes whose insulin requirement varied from 240 to 675 units daily. Evidence failed to indicate that a pituitary, adrenal, thyroid or gonadal influence was in any way responsible for the resistance. Wiener's [3] patient was rescued from coma by large doses of insulin. He had received as much as 3,250 units in twenty-four hours, probably the largest amount ever administered to a human being. The patient required large doses during the subsequent course of observation (five months). Glen and Eaton's [4] patient was given from 900 to 1,059 units daily for a period of twenty-seven days without appreciable effect on the blood sugar or glycosuria. Martin and his co-workers [5] treated a diabetic patient whose insulin resistance was apparently precipitated by hypersensitivity to protamine zinc insulin. He had received 6,375 units of insulin in eleven days, with 1,205 units as the highest dose in twenty-four hours. These authors, who collected 26 cases of insulin resistance from the literature up to 1941, call attention to the frequency with which allergy has been recorded in association with this condition. In the case reported by Regan, Westra and Wilder [6] a definite cause for resistance was not found. Administration of dihydroxyestrin was without effect. Glass and his associates [7] gave 85,000 units of insulin to a patient in a five and one-half month period. During episodes of ketotic acidosis it was necessary to give 2,360, 2,500 and 2,795 units of insulin in twenty-four hours before adequate control was accomplished. A definite cause for the insulin refractory state could not be determined. Therapeutic procedures included roentgen irradiation over the pituitary and the administration of lipocaic. However, it was not possible to establish a definite relation between these forms of therapy and the improvement which followed their use. The excessive need for insulin subsided six months after its onset and the patient remained mildly diabetic for the subsequent six months. Wayburn and Beckh's [8] patient was given from 500 to 2,460 units of insulin daily for four months. Although the patient was highly resistant to insulin, he nevertheless utilized insulin to some degree. A substance capable of elevating the blood sugar levels of rabbits was repeatedly demonstrated in the patient's blood. The authors assume the presence in the blood of this patient of an insulin antagonist substance.

Factors known to cause insulin resistance include acidosis, infections, sepsis, overactivity of physiologic antagonists of the pancreas, namely the pituitary, the thyroid and the adrenal glands, and liver diseases, in particular hemochromatosis. From the amount of insulin required to keep a depancreatized dog fed on ordinary diet, Root calculated that a man of average weight would require 200 to 300 units of insulin daily. Patients who require more insulin than this amount probably lack some factor other than insulin. The conception of insulin inadequacy as the cause of hyperglycemia, glycosuria and ketonuria has received much support from the success of insulin therapy. Although insulin has made it possible to restore diabetic patients to a normal state of carbohydrate metabolism, this substance may be only one of several factors in the complicated mechanism of the regulation of the carbohydrate metabolism. More recent researches, in particular those of Houssay and his co-workers, have established the role of the so-called diabetogenic factors of pituitary origin resulting in a disturbance of the normal regulation of carbohydrate metabolism.

1. Glassberg, B. Y.; Somogyi, Michael, and Taussig, A. E.: Diabetes Mellitus, Arch. Int. Med. **40**: 676 (Nov.) 1927.
2. Marble, Alexander: Insulin Resistance, Arch. Int. Med. **62**: 432 (Sept.) 1938.
3. Wiener, H. J.: Diabetic Coma Requiring an Unprecedented Amount of Insulin, Am. J. M. Sc. **196**: 211 (Aug.) 1938.
4. Glen, Alexander, and Eaton, J. C.: Insulin Antagonism, Quart. J. Med. **7**: 271 (April) 1938.
5. Martin, W. P.; Martin, H. E.; Lyster, R. W., and Strouse, Solomon: Insulin Resistance, J. Clin. Endocrinol. **1**: 387 (May) 1941.
6. Regan, J. F.; Westra, J. J., and Wilder, R. M.: Insulin Resistance, New England J. Med. **223**: 745 (Nov. 7) 1940.
7. Glass, W. I.; Spingarn, C. L., and Pollack, Herbert: Unusually High Insulin Requirements in Diabetes Mellitus, Arch. Int. Med. **70**: 221 (Aug.) 1942.
8. Wayburn, Edgar, and Beckh, Walter: Insulin Resistance in Diabetes Mellitus, J. Clin. Endocrinol. **2**: 511 (Aug.) 1942.

The anterior pituitary and the pancreas apparently act antagonistically in the control of the carbohydrate metabolism.

Wesselow [9] showed that the blood plasma of some elderly obese glycosuric patients, when injected into rabbits, would diminish the hypoglycemic action of insulin in a manner closely resembling that observed by other workers with extracts of the anterior pituitary gland. The plasma of young diabetic patients and of normal control subjects gave entirely negative results. This result suggests that the blood contains a substance with a diabetogenic action in certain cases of diabetes. Apparently lack of insulin is not always responsible for the disturbances of carbohydrate metabolism of the diabetic. Himsworth [10] has established, on the basis of his dextrose-insulin test, the existence of two types of diabetes mellitus, one in which the patient is insulin sensitive, apparently for lack of insulin, the other in which the patient is insulin insensitive for lack of an unknown factor which sensitizes the body to insulin. These patients are abnormal in being unable to react to an increase in dietary carbohydrates by an increase in their insulin sensitivity as the result of a lack of some unknown factor which in the normal subject produces sensitivity to insulin. In the case reported by Glen and Eaton, insulin tended to decrease sugar tolerance. Injection of the patient's serum into rabbits diminished their response to insulin and induced a degree of insulin antagonism. They therefore prefer the term "insulin antagonist" with reference to their case. The favorable effect of dihydroxyestrin was probably due to the antagonistic effect of this hormone on the anterior lobe of the pituitary, which then counteracted the production of the insulin antagonistic substance. It was logical to assume that the patient's blood contained a specific insulin antagonistic substance.

Insulin resistance and insulin antagonism are thus only one aspect of the complex problem of carbohydrate metabolism, involving as it does the liver with its glycogenic and glycolytic functions, and the synergistic and antagonistic effects of the various endocrine glands.

THIAMINE REQUIREMENT OF MAN

Several investigators have shown that the extent of urinary excretion of thiamine is an index of its status in the nutrition. In thiamine clearance studies in man Melnick and Field [1] demonstrated that all the subjects in their normal group, but none in the deficient group, excreted in excess of 50 micrograms of total thiamine during the four hour period following parenteral administration of 540 micrograms of thiamine.

Objective thiamine balance studies were made by Melnick [2] in man to detect the requirements for thiamine and the incidence of inadequate intake among apparently normal subjects. A study on 39 male and 33 female persons subsisting on adequate diets indicated good correlation between the urinary excretion of thiamine and the adequacy of the dietary level prior to conduction of tests. The normal person who consumes an adequate diet apparently tends to excrete part of the extra dietary thiamine in the urine. The deficient subject tends to conserve dietary thiamine to replenish depleted stores in the tissues and does not waste it by urinary excretion. When a test dose of thiamine was superimposed on the dietary intake, the extra vitamin was utilized like that obtained from the diet; it was conserved or wasted depending on the nutritional status of the subject.

This tendency of the depleted subject to conserve thiamine was observed in both the clinical and the experimental deficiency of thiamine. Thus the addition of thiamine to the inadequate diet to raise the level of intake to that of the normal group does not effect a parallel increase in the urinary thiamine excretion for a considerable period of time. Prompt response of normal subjects to variations in thiamine intake occurred while they were subsisting on their usual diets, which furnished approximately 1 mg. of thiamine daily. Apparently a constant daily intake of 1 mg. is sufficient to saturate the subject to such an extent that there is no necessity to conserve extra dietary thiamine. The recommended daily intake of thiamine is approximately 500 micrograms per thousand calories.

In a collateral study on 116 persons at the University Hospital, Ann Arbor, and at the Food Research Laboratories, Melnick showed that only 73 per cent of those apparently normal excreted in the normal range. The persons studied included mainly staff members of the hospital or laboratory personnel, whose diets were not restricted.

This high incidence of failures among so-called normal subjects to pass all the clearance tests, Melnick believes, is explained by the observations of Lane, Johnson and Williams at Summit, N. J., that the average American diet prior to the advent of enriched bread and flour furnished only 320 micrograms of thiamine per thousand calories. The observations of Melnick suggest that thiamine subnutrition is probably common even among persons who subsist on what is considered a normal diet. The correction, as was pointed out by Cowgill [3] as early as 1938, lies principally in improved diet. The problem calls for particular attention by the practicing clinician and students of preventive medicine, public health and nutrition.

9. de Wesselow, O. L. V., and Griffiths, W. J.: On the Possible Role of the Anterior Pituitary in Human Diabetes, Lancet **1**: 991 (May 2) 1936.

10. Himsworth, H. P.: Diabetes Mellitus, Lancet **1**: 127 (Jan. 18) 1936.

1. Melnick, Daniel, and Field, Henry, Jr.: Thiamine Clearance as an Index of Nutritional Status, J. Nutrition **24**: 131 (Aug.) 1942.

2. Melnick, Daniel: Vitamin B_1 (Thiamine) Requirement of Man, J. Nutrition **24**: 139 (Aug.) 1942.

3. Cowgill, G. R.: Human Requirements for Vitamin B_1, J. A. M. A. **111**: 109 (Sept. 10) 1938.

Current Comment

STRUCTURE OF BIOTIN

Success seems to have crowned the attempts of du Vigneaud of Cornell University Medical College and his collaborators to determine the exact chemical nature of biotin. The structural formula of this substance has now been published.[1] The compound is bicyclic and possesses a five membered urea ring, a ring containing sulfur in thio-ether linkage, and a fatty acid side chain. This chemical agent exerts a biologic effect in extremely great dilution and may be classed as one of the most active substances known. The growth promoting effect of biotin on an appropriate strain of yeast is noticeable when the factor is present in a concentration of only 1 part in 400 billion.[2] This may be compared with the dilating effect of epinephrine on the pupil of the frog eye, which can be demonstrated in a concentration of 1 in 20 million, and with the effect of thyroxin on the metamorphosis of the tadpole, which is demonstrable in a dilution of 1 to 5 billion.[2] This great potency alone makes biotin of unusual interest. However, the substance is also involved in animal metabolism and is recognized as a member of the vitamin B complex. Although human beings apparently require biotin,[3] this phase of the biotin problem has been relatively little studied and requires further investigation. Kögl and Tönnis, who first isolated biotin, obtained only about a milligram of the crystalline material from a fourth of a ton of dried egg yolks. While better methods of obtaining it from natural sources are now available, the substance is still difficult to prepare and is most costly. A more plentiful supply of biotin would facilitate further study and would undoubtedly lead to a fuller understanding of its function. The elucidation of the chemical makeup of biotin is an initial step in the direction of making the vitamin more readily available through synthesis.

1. du Vigneaud, Vincent: The Structure of Biotin, Science **96:** 455 (Nov. 20) 1942.
2. Kögl, F., and Tönnis, B.: Ueber das Bios-Problem, Ztschr. f. physiol. Chem. **242:** 43, 1936.
3. Biotin Deficiency in Man, Current Comment, J. A. M. A. **119:** 183 (May 9) 1942.

MICROCEPHALY AFTER PELVIC IRRADIATION DURING PREGNANCY

The possibility that exposure of the human ovary before conception or of the fetus in utero to radium or roentgen irradiation might be injurious has long been a matter of concern. Three types of exposure are recognized: therapeutic roentgen and radium irradiation of the ovaries prior to conception, diagnostic roentgen exposure of the fetus in utero and therapeutic roentgen and radium exposure of the fetus in utero. The therapeutic irradiation may be without effect on ovulation or it may cause temporary or permanent sterility. Evidence does not indicate, however, that such treatment has a deleterious effect on the health or development of infants if there is subsequent conception. During pregnancy the chief use for diagnostic roentgen irradiation lies in the field of pelvic mensuration. Thousands of such exposures have been made and evidence indicates that such irradiation is not detrimental to the infant. Finally, therapeutic amounts of radium and roentgen exposure are likely to be employed early in the life of the embryo, usually for the purpose of producing abortion. Such exposures have been followed by the birth of both normal and malformed offspring. Now Murphy and his colleagues [1] report a case in which embryonic irradiation was intentionally performed for the purpose of interrupting pregnancy. Previous to this occasion the mother had given birth to four bright, normally developed children. Irradiation did not produce abortion and the infant subsequently born, apparently at term and after normal labor, was microcephalic and at 14½ months was generally underdeveloped with an average mental age of 5.4 months. These workers point out that when pregnancy is not terminated in consequence of irradiation the physician or roentgenologist should insist that it be actually terminated—if not by the roentgen exposure then by some infallible means. From this study and the information previously available it is concluded that the human fetus should not receive large amounts of radium or roentgen irradiation. If fetal death or abortion does not follow such exposure immediately the pregnancy should be terminated at the earliest suitable moment.

1. Murphy, D. P.; Shirlock, Margaret E., and Doll, E. A.: Microcephaly Following Maternal Pelvic Irradiation for the Interruption of Pregnancy, Am. J. Roentgenol. **48:** 356 (Sept.) 1942.

THERAPEUTIC USE OF RADIOACTIVE SUBSTANCES

As pointed out by Low-Beer, Lawrence and Stone [1] in a study of the therapeutic effect of radiophosphorus, radiostrontium and radioiodine the problem of evaluation becomes difficult when one is dealing with chronic leukemia, since in this condition there is such great variation in length of life regardless of treatment. The distribution and metabolism of radioactive phosphorus in animal and human tissues indicate, they point out, that it should prove to be valuable as a therapeutic agent for some diseases, particularly chronic leukemia and polycythemia vera. In reporting its use on a carefully observed group of patients seen between 1937 and 1941 they conclude that radioactive phosphorus in sodium acid phosphate has proved to be of great value in the treatment of chronic lymphatic and myelogenous leukemias, polycythemia vera and lymphosarcoma. Its use in the treatment of Hodgkin's disease is not yet established by experience. Its place in the treatment of multiple myeloma and other conditions is also not well established, although the inevitably fatal outcome of these diseases justifies its experimental trial. The use of other radioactive elements such as strontium, iodine, element 85 and phosphorus in chromium phosphate appears to be of some value in certain conditions. Radioactive strontium, for example, is selectively taken up by the bones, and its role in the treatment of neoplastic disease of bone deserves to be and is being investigated. Likewise radioactive iodine 131 has proved effective in the treatment of hyperthyroidism but has not yet been tried on many patients. The further possibilities of using radioactive elements in various compounds which might localize in certain tissues, these investigators conclude, is unexplored territory with great potentialities.

1. Low-Beer, B. V. A.; Lawrence, J. H., and Stone, R. S.: The Therapeutic Use of Artificially Produced Radioactive Substances, Radiology **39:** 573 (Nov.) 1942.

MEDICINE AND THE WAR

In this section of The Journal each week will appear official notices by the Committee on War Participation of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medicine and the war and such other information and announcements as will be useful to the medical profession.

NEW PLANS FOR MEDICAL EDUCATION

Specialized Training Programs of the Army and Navy

The armed forces have need of the services of men with specialized training. They will utilize available facilities of certain American colleges to institute the training. Those receiving the training will be on active duty in uniform receiving pay and general military discipline. Arrangements will be made with various selected institutions for housing and messing facilities as well as for the actual training.

The plan here described has resulted from conferences between the Army, Navy, War Manpower Commission, and American Council on Education. The plan will be undertaken by the first three of these through a joint committee, with the final decisions in controversial matters being settled by the War Manpower Commission. Although it has been stated that the Army and Navy plans are similar, all data available at present indicate that there is considerable variation in the two programs.

THE ARMY

Selection will be governed by standards used for officers' candidate schools and some additional standards of the American Council on Education. Selection will be made from enlisted men who have completed or are completing basic military training and, except for some of the advanced courses, are under 22 years of age.

There are also eight special groups the members of which will be given training under this plan, including the following:

1. Medical students in the enlisted reserve, who will be called to active duty and detailed to continue instruction.
2. Medical students commissioned in the Medical Administrative Corps who may resign commissions and enlist as privates, to be detailed in the same manner as medical students in the enlisted reserve.
3. Premedical students in the enlisted reserve corps, who will continue on inactive status until the first semester of 1943 and will then be detailed as above.
4. Medical and premedical students not in the enlisted reserve who are taking approved courses, who will be inducted in Selective Service before the first semester of 1943, will be placed on inactive duty for a semester and then detailed for further training as above.

Colleges will be selected on the basis of standards, equipment, adequacy of housing and messing facilities, and minimum Army overhead. The standard of adequate proficiency is to be determined by the Army and the American Council on Education. Initial tests to predetermine the suitability of selectees will be evolved. Standard curriculums will be set by the Army and the American Council on Education. Military training will be given to these students during these courses of instruction under a cadet system. The plan will go into effect in February 1943 under the Commanding General of the Service of Supplies.

THE NAVY

Selection will be made of those having potential officer qualifications. Selections will be from high school graduates or the equivalent, from the seventeenth to the twentieth birthday, and enrolled or inducted men from the seventeenth to the twenty-third birthday. They will become apprentice seamen or privates in the U. S. Marine Corps on active duty with pay and will be assigned to designated colleges. Some other groups will also enter the training program, including V-1 or V-7 reservists who are undergraduates and qualify as medical, dental and theological students, who will continue on active duty as apprentice seamen under instructions in an accelerated curriculum in approved schools and seminaries until the completion of their professional studies.

Selectees can indicate the preference of their colleges and the branch of the service which they wish to join, including the Marine or the Coast Guard. Adequate arrangements for such students will be provided by the colleges under contract with the Navy, which will designate the number of students for the institution and the cost of maintenance of each student. The plan will be carried out under one naval officer in each institution, who will issue instructions as to discipline and routine. Outlines of curriculums will be released by the Bureau of Navy Personnel. Credits will be allowed for scheduled courses which have already been completed and substitution of courses permitted.

A special required minimum for premedical students is similar to standard premedical requirements of medical schools. If the students are qualified at the termination of their course, they will be commissioned in the appropriate reserve. The Navy has issued special details for the correlation of this program with existing programs and specific directions for those who are now in V-1, V-5 and V-7 reserves, Naval ROTC, or who are probationary commissioned students.

ARMY

TROPICAL MEDICINE SPECIALISTS

More than a hundred medical officers were graduated from the Specialists' Course in Tropical and Military Medicine at the Army Medical School, Washington, D. C., Dec. 12, 1942. Col. Richard P. Strong, director of the course and emeritus professor in tropical medicine of Harvard University, delivered the address. The diplomas were presented by Lieut. Col. Thomas T. Mackie, executive officer of the course. Col. George R. Callender, director of the Army Medical School, presided. The subcommittee on tropical medicine of the National Research Council of the National Academy of Sciences, of which Dr. Henry E. Meleney is chairman, cooperated in preparing the curriculum and in presenting a list of names of qualified specialists from which to select lecturers. This is one of many such courses recently completed at the Army Medical School. The next class, which will begin the course at once, will comprise more than a hundred medical officers as well as a group of civilians who are on the faculty of various medical schools and have been granted special permission to attend this course. The Markle Foundation is underwriting the expenses of the visiting medical school faculty members and is also assisting in making available to the

medical colleges instructional material for use in the undergraduate teaching program in tropical medicine.

The faculty for this course comprises especially qualified officers from various corps in the Army Medical Department, the Navy Medical Department, the U. S. Public Health Service and a civilian group appointed by the Secretary of War. The group from the Navy Medical Corps includes Rear Admiral Edward R. Stitt, retired, formerly Surgeon General of the Navy, Capt. Paul W. Wilson and Comdr. Leroy D. Fothergill. The group from the Public Health Service includes Drs. Edward Francis, Rolla E. Dyer, Louis L. Williams, Charles Armstrong, William G. Workman and Carl Larson. The civilians who thus far have participated as lecturers were Drs. Marshall A. Barber, Fred C. Bishopp, Mark F. Boyd, Walter Clarke, Lowell T. Coggeshall, William W. Cort, Ernest C. Faust, Thomas Francis Jr., William M. Mann, Henry E. Meleney, Elmer D. Merrill, Aristides A. Moll, Drs. John Scudder, Tom D. Spies, Max Theiler, Fred D. Weidman, Herbert C. Clark, E. Harold Hinman, Karl F. Meyer, George C. Shattuck, William H. Taliaferro, Ernest E. Tyzzer and Mr. William E. Riter.

In addition, special lectures were included in these courses when possible, and these have been given by Col. Frank S. Gillespie, British medical liaison officer, Medical Field Service School, Carlisle, Pa.; Major Gen. Alexander Gordon Biggam, chief adviser to the Director General, Medical Services, British Army; Col. N. Hamilton Fairley, director of medicine, Australian Army, and Dr. C. G. Pandit, Kings Institute, Madras, India.

COORDINATION OF INTERNSHIPS WITH THE ACCELERATED MEDICAL PROGRAM

The Surgeon General, U. S. Army, has issued general suggestions and recommendations pertinent to closer cooperation between hospitals approved for internship and the medical colleges under the accelerated medical program. The Surgeon General is loath to recommend that a graduate physician of an approved school be called to active duty with the armed forces prior to completion of a twelve months general rotating internship. It is obvious that if the hospitals approved for internships do not cooperate with the accelerated program it would lose its effectiveness in releasing men for duty with the Medical Corps as soon as anticipated. There is now an urgent need for young, physically qualified medical officers for field troop duty.

Original directives from the War Department indicated that graduates were allowed twelve to eighteen months for completion of essential internships. In many instances interns have interpreted this directive as being authority to utilize the additional time for hospital training before beginning the twelve month rotating internship. This has also allowed hospitals which customarily start their intern classes on or about July 1 of each year to maintain original schedules. It is believed that each hospital should establish a schedule of internships commencing on or about April 1, 1943, available to those who graduate in March 1943 under the accelerated medical program and thereafter as students graduate.

This obviously results in the doubling up of those who have not yet completed their twelve months beginning July 1, 1942, but it is hoped that these interns can be used in approved affiliated internships or in the capacity of subresidents to assist in the orientation of medical school graduates of March 1942. The most recent information available of the interns' situation indicates that there are excessive position vacancies over the supply of available interns.

Unless the situation demands it, the War Department does not desire to shorten the period of internship to less than the twelve months required. However, under the increasing pressure of our military needs it is necessary to expect graduates to be immediately available, if physically qualified, twelve months from the time of their graduation. The War Department does not feel that the eighteen months is necessary for completion of a twelve months internship, and this time will therefore no longer be allowed.

It is hoped that all interns will be trained in the rotating type of internship for the twelve months period; that is, one which provides training in medicine, surgery, pediatrics and their related subspecialties together with experience in laboratory and roentgenologic diagnosis. It is desired that house officers' positions be filled by those individuals not physically fit for military duty and those who are over age for troop duty. By following this procedure and increasing the duties of house officers and the essential staff membership, it is believed that a greater proportion of each year's intern class will be made available for active military duty.

Attention is invited to the new War Department directive precluding the appointment of senior medical students or interns as medical officers, Army of the United States, until within sixty days of their proposed active duty date. Such students and interns are protected from call to active duty by the War Department by:

1. Selective Service agreement.
2. Medical Administrative Corps commissions.
3. Commissions as Reserve Line officers, which they will receive on graduation from college.

This is accomplished under the authority of the War Department, A. G. O. letter dated May 8, 1942, subject "Commissions for Medical Students," the main purpose of which is to protect the essential medical training program.

RANK ON INITIAL APPOINTMENT

The Surgeon General of the Army has published from time to time detailed information concerning policies governing the initial appointment of physicians as medical officers, and dentists as dental officers.

FIRST LIEUTENANT ONLY FOR MEN UNDER 38

Because of changes occurring in the military situation and in the civilian requirements, it is contemplated that changes will be required in the standards for the initial grade of appointment of medical officers. It is anticipated that in the near future eligible physicians under the age of 38 years will be appointed in the grade of first lieutenant only and that physicians in the age group 38 to 45 will be appointed in numbers and in the grades for which position vacancies exist.

There is an acute need for medical officers under the age of 38. Applications are being solicited in those localities where physicians may be designated by the Procurement and Assignment Service as available for military service.

Appointments of medical and dental officers by medical officers' recruiting boards have been discontinued; however, the boards now active are to continue soliciting applications. All applications are forwarded to the Surgeon General for final recommendation of appointment.

MEDICAL INSPECTION OF SOUTHWEST PACIFIC AREA

Rear Admiral William Chambers, M. C., U. S. Navy, recently returned from a tour of inspection in the South and Southwest Pacific. In his thirty-six day trip made entirely by air, Admiral Chambers visited dressing stations on Guadalcanal, saw marines under treatment at hospitals in the New Hebrides and viewed the activities of the hospitals which the Navy has erected in New Zealand. The Surgeon General of the Navy, Rear Admiral Ross T. McIntire, M. C., recently disclosed that the mortality rate among wounded evacuated from the Solomons to mobile hospitals in the South Pacific was only 1 per cent for the first thousand men, which compares favorably with the normal expectancy of at least 5 per cent. The major share of credit for the low mortality in the Solomon campaign is given to the well equipped hospitals, the efficiency and fortitude of doctors and hospital corps men, blood plasma, sulfonamide compounds, tetanus toxoid and the speedy evacuation of the wounded. Ambulance planes also were given credit by Admiral Chambers, who said that each load carries as many as 11 litter patients and 4 or 5 sitting patients in addition to a medical officer, a pharmacist's mate and the crew. The situation is encouraging. The incidence of true dysenteries is low, and only 1 case of gas gangrene occurred on Guadalcanal while Admiral

Chambers was there. To illustrate that Navy doctors and hospital corpsmen attached to the Marines go where the fighters go, he said that two hands could be used to number our troops on Guadalcanal who have to use individual first aid dressings on themselves. Almost invariably when a Marine is wounded there is a surgeon or pharmacist's mate nearby. Admiral Chambers paid high tribute to Capt. T. Brown, Medical Corps of the Navy, Marine divisional surgeon on Guadalcanal, and Capt. Joel J. White, Medical Corps of the Navy, Commander of the advance hospital at Espiritus Santo, in the New Hebrides. This evacuation hospital, one of several in the Southwest Pacific to which wounded are flown, he said, is a stopover pending transfer of casualties to mobile hospitals southward by hospital ship.

EVACUATION HOSPITAL NO. 14 ON ACTIVE DUTY

THE JOURNAL, Dec. 12, 1942, page 1221, published an item entitled "Eight New York City Hospital Units on Active Duty" in which it was erroneously stated that U. S. Evacuation Hospital No. 14 (City Hospital Unit) was not on active duty. The information on which this item was based was from the New York *Times* of November 22. The commanding officer of Evacuation Hospital No. 14, Lieut. Col. Paul K. Sauer, writes that this hospital is at present on duty at Camp Claiborne, Louisiana, and that during the maneuvers, lasting one hundred and five days, this hospital, which is established completely in tents, treated 4,664 cases, among which were 221 major operations and 533 minor operations.

NAVY

EXPANSION OF PROGRAM FOR TRAINING NAVAL MEDICAL OFFICERS

Recommendations on expansion of the program for training naval medical officers in special fields were taken under advisement by Rear Admiral Ross R. McIntire, Surgeon General of the Navy, after a two day conference held December 10-11 at the Bureau of Medicine and Surgery. Submitted by the board of honorary consultants at the conclusion of the meeting, the report proposes:

1. Training of brain surgeons in naval hospitals, under Navy surgeons, with civilian hospitals and teaching personnel being utilized only if limited facilities make this step necessary.

2. Increasing the number of skilled anesthetists, to be achieved in part by training and utilizing medical officers of the Women's Reserve. (The commissioning of sixty women medical officers in the Waves has been authorized, such officers to be assigned to Women's Reserve training schools and stations.)

3. Supervision of optometrists by ophthalmologists — naval surgeons whose specialty is the eye.

Training of more medical officers in chest surgery, continued emphasis on physical therapy and the exercise of care in diagnosing neuroses also were urged by the consultants, whose report was drafted by Dr. Frank H. Lahey, Boston, head of the Lahey Clinic and chairman of the Procurement and Assignment Service.

Others attending the conference were Dr. Donald Church Balfour, director, Mayo Foundation, Rochester, Minn.; Dr. George W. Crile, director, Cleveland Clinic Foundation; Dr. Walter E. Dandy, professor of neurosurgery, Johns Hopkins Medical School; Dr. Oswald L. Lowsley, New York, and Dr. Willis B. Morse, Salem, Ore.; Dr. Wilbur A. Sawyer, New York, director, International Health Division, Rockefeller Foundation, and Dr. Meyer Wiener, St. Louis, professor of clinical ophthalmology, Washington University School of Medicine. Dr. George W. Crile was the only member of the board not present, because of illness.

MISCELLANEOUS

BRITAIN THANKS UNITED STATES DOCTORS FOR THEIR AID

At a luncheon given in honor of the heads of the United States and Canadian army medical services in England at St. Dunstan's, famed British home and training center for the blind, the minister of health, Ernest Brown, expressed Britain's gratitude to those American doctors who generously gave their services to Britain during the early days of the war. He described how a number of American doctors came at their own expense and without remuneration to help in British general and special hospitals in the earliest days of the war, and more arrived after the collapse of France. British medical facilities were open to the United States forces when they began to reach Britain, and it was arranged that any service personnel and other American nationals needing treatment should be accommodated in British emergency hospitals. Five new fully equipped hospitals were given over to the Americans and eight hospitals to the Canadians by the Health Ministry. Mr. Brown said that arrangements have been made at St. Dunstan's for its hospital and training center to care for blinded American soldiers awaiting evacuation, while Americans would treat British casualties across the Atlantic similarly.

ASCORBIC ACID (VITAMIN C) PLACED UNDER ALLOCATION CONTROL

Ascorbic acid (vitamin C) was placed under allocation control, December 15, through the issuance by the Director General for Operations of General Preference Order M-269. Development of the use of vitamin C in food and medicinal production for the armed forces was the primary cause for the action, as production was formerly geared to meet pharmaceutic needs. The present production does not meet current estimated requirements, and, although production capacity is being increased, demands for 1943 probably will be more than double the 1942 figures. Enough will be available, however, for essential civilian use. Vitamin C is used both by the armed forces and by civilians in the prevention and treatment of scurvy and other deficiency diseases caused by lack of sufficient quantities of this vitamin. The Quartermaster Corps is using large quantities in K and Jungle rations, and there is also a substantial demand for lend lease requirements. Sorbitol, recently placed under allocation control, is one of the principal raw materials needed for the production of vitamin C.

ARMY-NAVY E AWARDED TO WINTHROP CHEMICAL COMPANY

About a thousand employees and distinguished guests attended ceremonies at the plant in Rensselaer, N. Y., and at the offices in New York of the Winthrop Chemical Company, at which the Army-Navy E was presented to the Winthrop Chemical Company, which is manufacturing many vital drugs for the armed forces, among which is atabrine, synthetic substitute for quinine in the treatment of malaria. Atabrine is being manufactured in the United States today, said Dr. Theodore G. Klumpp, president of the company, at a rate of nearly one billion tablets a year. The flag was accepted for Winthrop's plant at Rensselaer by the plant superintendent, Dr. A. E. Sherndal. Dr. Klumpp in New York accepted the flag on behalf of the management. The principal speakers at the ceremonies were Brig. Gen. Charles C. Hillman of the Surgeon General's Office, Washington, D. C.; Rear Admiral Charles S. Stephenson of the Bureau of Medicine and Surgery, U. S. Navy; Dr. Morris Fishbein, editor of THE JOURNAL, and Lowell Thomas.

ORGANIZATION SECTION

OFFICIAL NOTES

ABSTRACT OF MINUTES OF MEETINGS OF BOARD OF TRUSTEES, NOV. 19 AND 20, 1942

A two day meeting of the Board of Trustees was held in November, preceded by a full day meeting of the Executive Committee.

A considerable part of the first day was devoted to a conference with representatives of the three national hospital associations for a discussion of problems of mutual interest. At this conference a committee consisting of Dr. James A. Hamilton and Dr. Bert W. Caldwell representing the American Hospital Association, Mr. Edgar Blake Jr. representing the American Protestant Hospital Association, Rev. Alphonse M. Schwitalla representing the Catholic Hospital Association and Dr. Ernest E. Irons and Dr. R. L. Sensenich of the Board of Trustees was appointed to prepare a preliminary draft of principles differentiating between the services that may be included in plans and in hospital bills and those that may not be so included.

ELECTIONS AND APPOINTMENTS

Dr. Mont R. Reid was elected to the Committee for the Protection of Medical Research and to serve as vice chairman.

Dr. R. A. Hatcher was appointed an honorary life member of the Council on Pharmacy and Chemistry with the privilege of the floor but without vote, and Dr. R. P. Herwick, chief of the Drug Division of the Food and Drug Administration, Washington, D. C., was elected to succeed Dr. Hatcher as a voting member of the Council.

A Committee on Student Health was appointed comprising Dr. J. E. Raycroft, Princeton, N. J. (chairman); Dr. A. V. Bock, Cambridge, Mass.; Dr. Ruth E. Boynton, Minneapolis; Dr. Frank B. Kelly, Chicago, and Dr. Oswald Nickoly Andersen, Stanford University, Calif.

WAR DAMAGE INSURANCE

The Board approved the purchase of war damage insurance to cover the headquarters of the Association, including buildings, machinery, equipment and inventories.

DATE OF MEETING OF HOUSE OF DELEGATES

The Board confirmed its mail vote that the first meeting of the House of Delegates be held on June 7, 1943.

MISCELLANEOUS

Considerable time was devoted to the matter of investments, and to other matters on which no definite action was taken and which will, without doubt, receive further consideration at a later date.

MEDICAL ECONOMIC ABSTRACTS

EXPANSION OF CALIFORNIA PHYSICIANS' SERVICE

The California Physicians' Service is steadily expanding the scope of its work into new fields. Some of these new fields are described in *California and Western Medicine* for November. The services had already undertaken the medical care of migrant agricultural workers, which is financed and its nonmedical features managed by the Farm Security Administration. The development of war industries has created a new migratory problem involving at least 150,000 workers. The Federal Public Housing Authority has constructed housing projects for these workers mostly in new areas which formerly had only a small population. Naturally physicians, hospitals and other medical facilities were lacking in these areas.

"The California Physicians' Service has been considering the problem for several months, and has offered a plan to the Federal Public Housing Authority to meet this need. In approaching the subject, several fundamental factors had to be considered:

"1. How to conserve the time of the already busy physicians.

"2. How to bring in more physicians to care for the increased population.

"3. How to relieve the load on the already overburdened hospitals.

"In May of 1942 the California Physicians' Service experimented with a plan in the Linda Vista Project in San Diego. The entire responsibility for developing a medical care program was assumed by C. P. S. Through its sales force an attempt was made to enroll families throughout the project in a prepaid medical care program. When a sufficient number had enrolled and adequate financing was in sight, then doctors and nurses would be placed on the project to serve the residents."

The sales cost in this experiment was found to be excessive and the demand for prepaid medical care was lacking. Nevertheless the placing of additional physicians by the California Physicians' Service did relieve the emergency load on the San Diego physicians.

"When the need for medical care became apparent in other projects throughout the state and C. P. S. was again consulted as to ways and means of meeting the situation. . . . Members of C. P. S. staff have been in constant consultation with the staff of the Federal Public Housing Authority and with representatives of the United States Public Health Service."

The new plan includes the responsibility of the Federal Public Housing Authority to enroll members in California Physicians' Service on a voluntary prepaid basis. Dues are collected when rent is paid. This permits the California Physicians' Service to concern itself with supplying necessary physicians and nurses and to arrange for hospitalization with Blue Cross Hospital Associations. This plan is now being developed in the new housing project in Marin City. There are only two physicians and no hospital closer than 15 miles to this area, in which approximately 7,000 new residents will be introduced. This is another example of the collaboration of the medical profession and various governmental agencies.

The California Medical Service is also cooperating with a rural health program involving farm families with a net income of $2,000 or less. It is expected that about four thousand farm families in Tulare County may be included in this program. Steps are also being taken to establish a similar plan in Fresno County.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

CALIFORNIA

Changes in Faculty at Stanford.—Dr. William E. Stevens recently retired from the faculty of Stanford University School of Medicine, San Francisco, with the title associate clinical professor of obstetrics and gynecology, emeritus. Dr. Stevens graduated at the Medical Department of the University of California in 1899 and has been a member of the faculty at Stanford since 1919. New appointments to the faculty include those of Drs. Henry Dean Brainerd as clinical instructor in medicine and pediatrics, James B. Irwin instructor in neuropsychiatry and Robert P. Watkins clinical instructor in bone and joint surgery, all of San Francisco.

"Impostor Phillips" Sentenced to Five Years.—Arthur Osborne Phillips was sentenced to a term of five years in a federal penitentiary, December 10, after pleading guilty to falsifying government records to secure employment as a CCC physician. According to the San Francisco *Call-Bulletin*, Federal Judge Martin I. Welsh meted out terms of five, three and three years on the three of four counts in a grand jury indictment to which Phillips pleaded guilty but ruled that the sentences should run concurrently. Phillips had been in the Sacramento county jail since his release on November 27 from the Butte county jail, where he had been serving a nine months sentence for practicing medicine without a license at Enloe Hospital, Chico, and for being a former convict in possession of a gun. He had been paroled to federal authorities "after the Butte County board had decided to withdraw their hold on him since he was sought by the federal government." Phillips, who was reported to have admitted that he performed thirty-two appendectomies since September 1941, was classified as a surgeon at the Brush Creek CCC camp before joining the staff of Enloe Hospital, it was stated. A complete record of Phillips's activities was published in THE JOURNAL, Sept. 12, 1942, page 145.

DELAWARE

Cancer Work Extended.—At a meeting of the executive committee of the Delaware State Committee of the American Society for the Control of Cancer, the constitution of the state group was amended to broaden the scope of its activities. In addition to its educational purposes the group will now aid patients in financial straits to receive proper diagnosis or treatment, assist in the establishment, development or maintenance of hospital clinics, laboratories or other facilities for the care of cancer patients, and generally carry on cancer control activities except the actual treatment of patients or actual operation of hospitals, clinics, laboratories or other facilities for such treatment. Rather than launch new projects at this time, particular attention will be given to the plan to render financial aid to special cases started more than a year ago. A simple method of procedure has been evolved whereby county commanders of the field army have been given a drawing account, and cases referred to them will receive immediate attention. Cases must be presented by accredited physicians and receive the approval of either the county chairman or some other medical member of the executive committee. Physicians are asked to cooperate with the state committee by investigating causes of delay in cancer treatment. The state medical journal points out that, if it is financial worry which deters the patient, the case should at once be reported to the county commander of the field army. The three county commanders are: Kent, Mrs. Lincoln Clayton, Dover; New Castle, Mrs. William N. Cann, Wilmington; Sussex, Mrs. Topp M. Heath, Frankford. The county chairmen of the executive committee are Drs. Clarence J. Prickett, Smyrna; Charles E. Wagner, Wilmington, and John Roscoe Elliott, Laurel. The state headquarters are located at the Delaware Academy of Medicine, Wilmington.

GEORGIA

Pediatric Meeting.—The Georgia Pediatric Society held its annual scientific meeting in Atlanta, December 10. The afternoon session will be in the Biltmore Hotel and the evening session at the Academy of Medicine. The speakers included:

Dr. Alexander A. Weech, Cincinnati, Significance of Protein in the Diet and Cortical Maturation and the Development of Behavior in Infants.

Dr. Meredith F. Campbell, New York, Persistent Urinary Infection in the Young and Surgical Treatment of Certain Common Urologic Conditions in Children.

Dr. Abraham Levinson, Chicago, Neurologic Disturbances of the Newborn and Value and Limitations of Spinal Puncture in Children.

ILLINOIS

Dr. Pettitt Named Chief of the Emergency Services.—Dr. Herbert L. Pettitt, Morrison, who recently resigned as assistant state health director to resume private practice (THE JOURNAL, Nov. 7, 1942, p. 774), has been appointed chief of emergency medical services in the Illinois Defense Council. The position was formerly held by Dr. Roland R. Cross, Springfield, state health director. Dr. Pettitt will devote only part time to the position.

Chicago

Society News.—The North Shore Branch of the Chicago Medical Society will be addressed on January 5 by Drs. Douglas N. Buchanan and Charles Anderson Aldrich, on "Diagnosis of Acute Cerebral Conditions in Children" and "Color Photography in a Pediatric Clinic" respectively.——At a meeting of the Chicago Laryngological and Otological Society on January 4 the speakers will be Drs. Lawrence J. Lawson, Evanston, Ill., on "Carcinoma of the Eustachian Tube"; Leopold B. Bernheimer, "Otolaryngological Neoplasma—Clinical report of cases," and Paul H. Holinger and H. James Bara, Hinsdale, Ill., "Bronchogenic Carcinoma—Diagnostic Studies in 150 Cases."

Lectures at Institute for Psychoanalysis.—A series of lectures and seminars will be held at the Institute for Psychoanalysis. Registration should be made prior to January 5. The lectures for professional or lay groups will consist of "Introduction to Fundamental Principles of Psychoanalysis and Psychosomatic Medicine" by Dr. Franz G. Alexander and "Personality Development in Childhood and Adolescence" by Helen Ross, B.S., and Dr. George J. Mohr. For members of the Chicago Psychoanalytic Society and students of the institute the topics to be considered are mechanisms of the individual neuroses, Freud's interpretation of dreams, selected problems of technic, clinical conferences on children's cases, review of psychoanalytic literature and clinical conferences. Lecturers will be Drs. Alexander, Thomas M. French, Edward Weiss, Margaret W. Gerard and Helen Vincent McLean.

KENTUCKY

Addition to Tuberculosis Sanatorium.—A 96 bed addition to the Waverly Hills Sanatorium, Waverly Hills, is now under construction at a cost of about $160,000. The addition will serve to bring the beds available for Negroes with tuberculosis up to a level of about 2 per annual Negro death. This ratio is already achieved for white patients, it is reported. Funds are being supplied jointly by the city of Louisville and by Jefferson County. The sanatorium is administered by the Louisville and Jefferson County Health Department.

MASSACHUSETTS

Personal.—Dr. Winthrop B. Osgood, Boston, has been appointed medical superintendent of the Memorial Hospital, Worcester, succeeding Dr. George H. Stone, who has resigned because of ill health.

Students to Serve as Hospital Aids to Relieve Shortage.—Boston University students will serve as interns, kitchen workers and nurses' aides in Boston hospitals on a part time basis while attending college during the new year to help relieve the serious shortage of help in local institutions through a "hospital emergency service" sponsored by the University Student Defense Board. Students will register with the board indicating the hours they can spare each day for hospital work and will be assigned to institutions in Boston through the Boston Red Cross headquarters.

MISSOURI

Personal.—Dr. John L. Myers, Kansas City, was presented with a wrist watch during the meeting of the American Academy of Ophthalmology and Oto-Laryngology in appreciation of his sixteen years' service as a section secretary of the academy.

Special Society Election.—Dr. Elmer E. Glenn, Springfield, was recently chosen president of the Missouri Tuberculosis Association at its meeting in St. Louis, and Drs. Herbert L. Mantz, Kansas City, and Newell R. Ziegler, Columbia, were named vice presidents. Drs. Jesse E. Douglass, Webb City, James Stewart, Jefferson City, and Jesse A. Stocker, Mount Vernon, were elected members of the executive committe.

State Board Reorganized.—The Missouri State Board of Health was reorganized at a meeting in Jefferson City, December 7. Dr. Cleveland H. Shutt, St. Louis, was elected president, Dr. Charles H. Neilson, St. Louis, was elected vice president and Dr. James Stewart, Jefferson City, state health

commissioner, was elected secretary. Prior to the reorganization of the board Dr. Stewart and Drs. Hardin M. Henrickson, Poplar Bluff, and Howard B. Goodrich, Hannibal, were chosen members of the board.

NEW JERSEY

New Rehabilitation Center for Women with Venereal Diseases.—The state department of health has approved plans to use the former home of Mr. and Mrs. Charles A. Lindbergh, Hopewell, as a hospital and rehabilitation center for women infected with venereal diseases. The state accepted the Lindbergh home as a gift more than a year ago.

Society News.—Dr. Clarence R. O'Crowley, Philadelphia, discussed "Anomalies of the Kidneys and Polycystic Disease of the Kidneys" before the Passaic County Medical Society on December 15.——Major Henry A. Cotton Jr., Trenton, discussed "Psychiatric Problems in the Armed Forces" before the Morris County Medical Society at Greystone Park, October 15.

Intestinal Outbreak Among Infants.—An intestinal infection, attributed to a virus, has affected 30 infants in the maternity ward in Holy Name Hospital, Teaneck, newspapers reported December 16. Two deaths occurred. The chief result of the ailment appeared to be dehydration. The infants were transferred to the pediatrics department of the hospital, which has been isolated and closed to new cases, but the maternity ward is accepting new cases under restrictions.

NEW YORK

Age of Physicians Attending Meetings.—The Medical Society of the State of New York has issued a release on the comparison of attendance this year with last at district branch meetings, covering the entire state and comprising postgraduate educational activities. In 1941 the attendance at corresponding meetings of physicians between 45 and 54 years of age consisted of 25.21 per cent of the total; in 1942, 30.81 per cent. From 55 to 64 years, 16.15 per cent in 1941 and 22.56 in 1942. Among those from 65 to 74, 9.79 per cent in 1941 and 15.66 in 1942. In the group 75 to 84, 1.56 per cent in 1941 and 2.53 in 1942.

The Kenny Technic.—Dr. Philip M. Stimson, New York, will deliver a lecture, January 5, on "The Early Treatment of Poliomyelitis with a Description and Evaluation of the Kenny Technics." The meeting will be a joint session of the Onondaga County Medical Society and the Syracuse Academy of Medicine, under the auspices of the state medical society and the state department of health. On December 15 the Albany County Chapter of the National Foundation for Infantile Paralysis sponsored a free demonstration of the Kenny method. Dr. Don W. Gudakunst, medical director of the National foundation, New York, was the principal speaker.

Safeguard Against Accidents.—The New York State Public Welfare Council has adopted an amendment to the sanitary code, effective March 1, prohibiting the sale, distribution or use of any poisonous substance as an exterminator or insecticide unless the container bears a label legibly and conspicuously printed with the words "Poison" and the symbol of the skull and crossbones in red ink followed with the words "Caution—this exterminator or insecticide contains [state the name of the poison], a deadly poison" together with the antidote and treatment therefor and the name and address of the manufacturer or packer, and the words "poison," "caution" and "antidote" in block type of a larger size than the other wording. Insecticides or exterminators containing a fluoride shall be colored nile blue, as designated by Ridgeway's Color Standards and Nomenclature, and, if sold at retail in quantities of 5 pounds or less, the container thereof shall be of a nonrefillable type. The amendment was adopted as a safeguard against accidents such as the one that occurred recently at the Oregon State Hospital, Salem (THE JOURNAL, Nov. 28, 1942, p. 1050). Other examples cited to account for the new amendment were an outbreak in an upstate institution of 69 cases of food poisoning, which was traced to the accidental introduction of sodium fluoride into chocolate pudding, and twelve fatal poisonings in the state of Maryland, which were the result of mistaking sodium fluoride for pancake flour.

New York City

County Society Approves Plan to Examine High School Boys.—The Medical Society of the County of Kings has approved a plan inaugurated by the board of directors of the Society of New York whereby high school boys 16½ years and older, the preinduction age group, are expected to go to their family physician for a thorough physical examination preparatory to permitting these pupils to engage in a physical fitness program. Every effort will be made by the high schools to induce these boys to obtain the physical examination from their family physician, but, in the event that some boys have no private physician and cannot pay the usual examination fee, volunteer physicians will be asked to make the examination in their offices. The plan is only for older boys and only for the duration. A roster of physicians offering to participate in the plan is being prepared by the director of medical activities of the Medical Society of the County of Kings. Each high school will be given a copy of this roster and each boy will be given an opportunity to select his own physician. Each high school will assume the responsibility for the follow-up care of defects discovered in the physical examination, through referral to the boy's own physician wherever possible, and, if not possible, to municipal clinics.

Health Education Conference.—The 1942 Health Education Conference of the New York Academy of Medicine was held on November 17 with Dr. Malcolm Goodridge, then president of the academy, presiding. Among the speakers were:

Dr. Cassius H. Watson, The Wartime Intensive Industrialization in the Community and Its Health Implications.
Otto A. Bessey, Ph.D., Food and Nutrition in the Home and in the Work Place.
Dr. Leonard Greenburg, Disease and Handicap Detection and Control in Industry.
Dr. Lydia G. Biberson, Mental Problems and Morale in Industry.
Mr. Harold R. Bixler, Educational Methods and Control of Accidents in Industry.
Dr. Iago Galdston, Summary and Review of Conference.

Friday Afternoon Lectures.—The regular series of Friday afternoon lectures which opened November 6 at the New York Academy of Medicine will include the following speakers:

Dr. Russell C. Grove, January 8, Present Concepts and Treatment of Sinusitis.
Dr. David M. Bosworth, January 15, Shoulder Pain and Disabilities.
Dr. Milton C. Peterson, January 22, Indications and Contraindications for the Newer Anesthetic Agents.
Dr. S. Bernard Wortis, January 29, Modern Treatment of the Psychoses.
Dr. Byron P. Stookey, February 5, Intractable Pain—Surgical and Medical Treatment.
Dr. Robert L. Levy, February 19, Clinical Types of Coronary Insufficiency and Their Recognition.
Dr. Maurice Bruger, February 26, Recent Advances in the Clinical Interpretation of Laboratory Data.
Dr. Philip Levine, Newark, N. J., March 5, The Role of the Rh Factor in Erythroblastosis, Transfusion and Accidents and Its Importance to the Obstetrician.
Dr. Albert H. Aldridge, March 12, Toxemias of Pregnancy.
Lieut. Comdr. Harold J. Harris, M. C., U. S. Naval Reserve, Westport, N. Y., March 19, Brucellosis: Diagnosis, Differential Diagnosis and Treatment.
Dr. M. Henry Dawson, March 26, Rheumatoid Arthritis and Its Treatment, Including Gold Therapy.
Dr. Ralph Colp, April 2, Postcholecystectomy Syndrome.
Dr. Henry L. Jaffe, April 9, Phosphatase Values in Relation to Bone Diseases.
Dr. Maurice Lenz, April 16, Value of Roentgen Therapy in Inflammatory Conditions.

OHIO

Megrail Collection at School of Medicine.—Friends of the late Dr. Emerson Megrail, associate professor of hygiene and bacteriology at Western Reserve University School of Medicine, Cleveland, are invited to contribute books to the Megrail Collection, which has been placed in the students' room of the medical school. An appropriate bookplate has been designed by Dr. Louis J. Karnosh, associate clinical professor of nervous diseases at Western Reserve. Reprinted classics of medicine, monographs, biographies of physicians and scientists and semipopular books on medical subjects are especially desired. To avoid duplication, donors are requested to phone or write to the secretary of the department of hygiene and bacteriology at the school. Dr. Megrail had been a member of the staff of Western Reserve from 1919 until his death on Oct. 21, 1941.

Night Service Plan Adopted by Medical Society.—The Montgomery County Medical Society recently approved a plan for improving the night emergency medical care for pay patients, especially to take care of the emergencies arising at night among persons who have newly arrived in the locality or patients of the physicians who have joined the armed forces and have no medical connection. It is a war emergency plan only. Steps have been taken to have a night clerk in the city building to obtain all personal data between the hours of 10 p. m. and 6 a. m., the call to be referred by the clerk to the physician. Physicians will be stationed at the receiving ward of each hospital to receive the necessary hospital cases or to make house calls where absolutely necessary. This service is to be independent of the regular routine hospital service. Special stipulations cover the retaining of the physician making the call. Written reports are to be made out for reference

for the hospital, the Montgomery County Medical Society and the doctor who has to take care of the patient in the future. The society approved special minimum rates to care for every emergency. According to an announcement it is hoped that all physicians will be willing to participate in the plan, but the county society voted that the service of the physicians should be on a voluntary basis. The method of supervision and directing the program is to be under the guidance of the executive council of the society.

Lawyer Named Head of Cleveland Clinic Foundation.—Edward C. Daoust, for more than twenty-five years a member of the firm of Garfield, Daoust, Baldwin & Vrooman, retired from the practice of law on January 1 to become the full time executive head of the Cleveland Clinic Foundation, which owns the Cleveland Clinic and its hospital. As foundation president Mr. Daoust will succeed Henry S. Sherman, president of the Society for Savings, who will become president of the board. A. C. Ernst will continue as vice president and G. W. Gill and Remington Peck are secretary and treasurer, respectively. The clinic foundation is chartered as a nonprivate institution, operated for scientific, charitable and educational purposes. It employs 656 persons, including a staff of 69 physicians and surgeons. The principal properties are a 275 bed hospital and an eight story building that is devoted to experimental medicine and research. The cost of buildings and equipment exceeds $3,500,000 and the foundation's endowment funds for medical research and charitable service are close to $1,500,000. After the war the foundation plans to erect additional stories on the new Cleveland Clinic Building, which has foundations to support fourteen floors. The clinic was founded in 1921 by Drs. George W. Crile, William E. Lower and the late Drs. Frank E. Bunts and John Phillips. Mr. Daoust began the practice of law in Cleveland following his graduation from Yale University, New Haven, Conn.

OKLAHOMA

Personal.—Dr. Hugh M. Galbraith, Oklahoma City, has been named a member of the medical advisory committee of the state medical association to the state department of public health, succeeding Dr. Moorman P. Prosser, Norman, who has entered military service.

Circuit Course in Internal Medicine.—The fifth circuit in postgraduate medicine will open in Oklahoma City, Norman, Pauls Valley, Shawnee and Wewoka or Holdenville the week of January 11, according to the state medical journal. Dr. Luke W. Hunt, Oklahoma City, has been giving these courses throughout the state under the auspices of the Commonwealth Fund of New York (THE JOURNAL, Feb. 21, 1942, p. 658). The lectures will cover the subjects of chronic arthritis and allied conditions, gastrointestinal diseases, disorders of the heart, cardiovascular renal disease, the anemias and blood dyscrasias, chronic nontuberculous pulmonary disease, diabetes mellitus, the uses and abuses of the sulfonamide compounds, nutritional diseases and deficiency states and endocrine disorders.

PENNSYLVANIA

Outbreak of Smallpox Among the Amish.—A quarantine has been placed on an area of 40 square miles of Kishacoquilias Valley in an effort to halt an outbreak of smallpox believed to have stemmed from an Amish wedding, the New York *Times* reported on December 26. Seven Amish children, including 3 year old twins, were reported on December 25 to be suffering from smallpox, the first children stricken in the Amish farm section. On December 24 twenty adults between the ages of 50 and 70 were reported with the disease and all had been present at the Amish wedding several weeks ago. None of the child victims had been vaccinated and all are under school age. Many of the Amish adults had not been vaccinated. The inoculation is compulsory for their children, however, under state school laws. All social gatherings and Christmas church services were canceled in the valley of 8,200 inhabitants. State police guarded all roads leading from the area. The Lewiston farmers' market was forced to close, leaving unfilled hundreds of orders for turkeys from Amish farmers. A woman guest from Ohio was suspected of having been the carrier. An Associated Press dispatch from Columbus, December 25, indicated that the woman was the wife of a minister who had been in good health before taking a three week trip with her husband into Pennsylvania, Delaware and Maryland to attend several weddings. She became ill with smallpox on her return late last month, it was stated. While members of the Ohio sect opposed vaccination, they submitted to immunization after 4 cases of smallpox were reported.

Philadelphia

Lectures on Legal Medicine.—The Philadelphia County Medical Society announces a series of lectures on legal medicine, January 8 to March 12, to be conducted by the office of the coroner of Philadelphia County. The series includes:

Drs. Benjamin A. Gouley and Edward B. Krumbhaar, Causes of Sudden Death.
William J. Connelly and Edward J. Burke, Identification.
Lieut. George R. Spangler, Ballistics.
Dr. Edward A. Strecker, Suicide.
Charles J. Swalm and James W. Tracey Jr., Criminal Assault.
Dr. Elizabeth D. Wilson, Asphyxiation, Drowning and Burns.
Ivor Griffith, Ph.M., and Helen Ingleby, M.B., Ancient and Modern Poisons.
Dr. Frank W. Konzelmann, Ancient and Modern Poisons (continued).
Dr. Abraham M. Ornsteen, Insanity.
Judge Byron A. Milner, The Government and the Physician.

Pittsburgh

Society News.—Dr. Joseph T. Beardwood Jr., Philadelphia, addressed the Allegheny County Medical Society, December 15, on "Management of Diabetic Emergencies" and Dr. Angelo L. Luchi, Wilkes-Barre, "Diabetic Diets and Food Habits of the Nationalities."

Industrial Health and Hygiene.—The University of Pittsburgh School of Medicine and the Allegheny County Medical Society are cooperating in a series of lectures on industrial health and hygiene. The series opened on December 10 and will continue on successive Thursdays. Drs. Frank S. Rossiter, Swissvale, Pa., and Dr. Lawrence G. Beinhauer gave the first lectures on "Carbon Monoxide Poisoning" and "Occupational Dermatitis" respectively. On December 17 the speakers were Henry F. Smith Jr., Ph.D., on "Volatile Solvents" and Dr. George J. Busman, "Differential Diagnosis and Treatment of Occupational Dermatoses." The third pair of lectures will be given on January 7 by Drs. Charles F. Engel, Homestead, Pa., on "Electricity, Physiological Effects, Systemic and Local Treatment" and Charles F. Kutscher, "Eye Injuries: Diagnosis and Treatment."

SOUTH CAROLINA

Faculty Changes at South Carolina.—William A. Prout, Phar.D., has been named acting director of the school of pharmacy of the Medical College of the State of South Carolina, Charleston. He will continue as professor of operative pharmacy. Morris Belkin, Ph.D., formerly at Yale University School of Medicine, New Haven, Conn., has been appointed instructor in pharmacy at the school.

Founders Day Exercises.—The Founders Day Exercises at the Medical College of the State of South Carolina, Charleston, were held November 4-5 in connection with a refresher course sponsored by the alumni association. Visiting lecturers included Drs. Robert B. Greenblatt, Augusta, Ga.; John B. Youmans, Nashville, Tenn.; Dr. Udo J. Wile, Ann Arbor, Mich.; Luther E. Holt Jr., Baltimore; William B. Porter, Richmond, Va.; Reginald Fitz, Boston, and James Heyward Gibbes, Columbia; Major George K. Lewis and Captain Alfred J. Suraci, M. C., U. S. Army; Dr. Howard T. Karsner, Cleveland, delivered the Founders Day Lecture at the annual banquet, on "Aortic Stenosis."

TENNESSEE

New Hospital in Memphis.—The Thomas Frank Gailor Psychiatric Hospital and Diagnostic Clinic was recently officially dedicated as part of the John Gaston Hospital, Memphis. It will be staffed by the University of Tennessee College of Medicine and, except for staff salaries, operating expenses will be handled through the Memphis and Shelby County Health Department. City, county and state funds were used to finance the cost of $515,000. Four floors of the six story building will be used as an outpatient clinic and two as a psychiatric hospital. Three floors of the hospital have 40 beds available, 30 to be used for the care of temporary patients and 10 for teaching purposes. Dr. Theron S. Hill, professor of psychiatry at the University of Tennessee College of Medicine, is director of the new hospital. Dr. Arthur F. Cooper, Memphis, secretary of the Memphis and Shelby County Medical Society, has been named the first full time director of the outpatient portion of the new unit.

TEXAS

Professor of Dermatology Appointed.—Dr. Chester N. Frazier, recently engaged in venereal disease control work at the Johns Hopkins School of Hygiene and Public Health, Baltimore, has been appointed professor of dermatology and syphilology at the University of Texas Medical Branch, Galveston. Dr. Frazier was formerly professor of dermatology and syphilology at Peiping Union Medical College, Peiping, China, where he had been a member of the staff since 1922.

University News.—Dr. Owen H. Wangensteen, professor of general surgery, University of Minnesota Medical School, Minneapolis, delivered the Alpha Omega Alpha lecture at the University of Texas Medical Branch, Galveston, recently on the "Secretory Functions of the Appendix as a Factor in Appendicitis." At the banquet Dr. Wangensteen discussed "Surgical Aspects of Peptic Ulcer." The staff and students at the medical branch were recently addressed by Dr. Meyer Wiener, Coronado, Calif., professor of clinical ophthalmology emeritus, Washington University School of Medicine, St. Louis, on "War Injuries to the Eye."

GENERAL

Katharine Lenroot Awarded Medal.—The Rosenberger Medal for "notably great service in the promotion of human welfare" was awarded to Katharine Lenroot, Washington, chief of the Children's Bureau, U. S. Department of Labor, during the two hundred and eleventh convocation of the University of Chicago in Rockefeller Memorial Chapel, December 18.

Academy of Pediatrics Opens Membership to Latin Americans.—At the annual meeting of the American Academy of Pediatrics in Chicago, November 4-7, it was decided to develop region 5 of the academy to consist of the Latin American countries, members to be taken in practically on the same basis as members from the United States. On November 6, fifteen Mexican pediatricians who had applied were accepted to form the basis of a group in Mexico. According to Dr. Clifford G. Grulee, Evanston, Ill., secretary of the academy, steps are now being taken to develop groups in each of the Latin American countries from which communications have already been received. The names of the Mexican pediatricians who were recently elected to membership are Drs. Alfonso G. Alarcón, Rigoberto Aguilar Pico, Alejandro Aguirre Torres, Enrigue Baz Dresch, Hermilo Lamberto Castañeda L. Federico Gomez Santos, Deñofilo Gonzalez C., Carlos Herrera Romero, Fernando Lopez Clares, Jesús Lozoya Solis, Ismael Martinez Sotomayor, Jorge Muñoz Turnbull, Agustín Navarro Hidalgo, Roberto L. Sanchez Messick and Rafael Soto Allande, all of Mexico, D. F.

Reorganization of International Society of Surgery.—The headquarters of the International Society of Surgery has been provisionally transferred from Brussels to the United States and set up in the Inter-American Division of the New York Academy of Medicine, in accordance with recent action of the council of delegates. In explaining the need for the change, Dr. Rudolph Matas, New Orleans, acting secretary and treasurer, stated:

> The German occupation of Belgium and the Nazi devastation of the rest of Europe and all the other war-torn nations had virtually restricted the international relations of the society to the Western Hemisphere, where its fellowship is widely spread through its affiliated branches in North, Central and South America.
>
> The Executive Committee of the United States Division, the largest, most active contributor to the transaction, felt it their duty conjointly with their Latin American colleagues to rescue the society from the perils of the European conflagration. The first steps were taken in November 1941, at Boston, but no final action could be taken to transfer the official sanction in Brussels to America without the concurrence and approval of all the affiliated branches in America.

The transfer was voted by the delegates from all the affiliated societies of the Americas, representing Argentina, Brazil, Canada, Cuba, Ecuador, Guatemala, Mexico, Paraguay, Peru, the United States, Uruguay and Venezuela. The affairs of the society will be administered by an executive committee composed of Colonel Elliott C. Cutler, M. C., U. S. Army, chairman in absentia; Dr. Eugene H. Pool, New York; Dr. Arthur W. Allen, Boston, and Dr. Matas. Dr. Pool is acting chairman for Colonel Cutler and Dr. Jose Arce, dean of the University of Buenos Aires, is acting president in the absence of Prof. Leopold Mayer, Brussels, detained in Belgium by Nazi compulsion, according to *Science*. A revision of the constitution prepared by Dr. Matas was adopted in November and a representative group of fellows from New York and elsewhere signed the act of reorganization as witnesses of the signing of the act by the delegates of the governing council. The Inter-American Division of the New York Academy of Medicine is under the direction of Dr. Mahlon Ashford, New York. Dr. Enrique J. Cervantes, New York, assistant secretary-treasurer of the executive committee of the international society, editor of *America Clinica*, the official organ of the society, and secretary of the Hispanic-American Medical Society, is available in the division's offices to render service to the fellows of the society and to medical visitors from the Latin American countries.

Examinations in Obstetrics and Gynecology.—The next written examination and review of case histories (part I) for all candidates will be held in various cities of the United States and Canada on Saturday, February 13, at 2 p. m. Arrangements will be made so far as possible for candidates in military service to take the part I examination (written paper and submission of case records) at their places of duty, the written examination to be proctored by the commanding officer (medical) or some responsible person designated by him. Material for the written examination will be sent to the proctor several weeks in advance of the examination date. Candidates for the February 13 part I examination who are entering military service or who are now in service and may be assigned to foreign duty may submit their case records in advance of the aforementioned date by forwarding the records to the office of the board secretary. All other candidates should present their case records to the examiner at the time and place of taking the written examination. The Office of the Surgeon General of the U. S. Army has issued instructions that men in service, eligible for board examinations, be encouraged to apply and that they may request orders to detached duty for the purpose of taking these examinations whenever possible. All candidates will be required to take both the part I examination and the part II examination (oral-clinical and pathology examination). Candidates who successfully complete the part I examination proceed automatically to the part II examination which will be held in Pittsburgh, May 19-25. Notice of the exact time and place of the examinations will be sent all candidates well in advance of the examination date. Candidates in military or naval service are requested to keep the secretary's office informed of any change in address. If a candidate in service finds it impossible to proceed with the examinations of the board, deferment without time penalty will be granted under a waiver of published regulations applying to civilian candidates. Applications are now being received for the 1944 examinations of the board. For further information and application blanks, address Dr. Paul Titus, secretary, 1015 Highland Building, Pittsburgh, Pa.

Activities at North China Drug Factory.—During the first eight months of the current year, 350,000 tubes of smallpox vaccine were manufactured at the "guerrilla drug factory" in Northwest China, according to a release from the United China Relief, New York. Credit is given largely to the work of this drug factory for averting a major smallpox epidemic, the release states. The factory was opened four years ago in the center of a plague belt where epidemics of typhus, diphtheria and typhoid are common. The plant is assisted financially by United China Relief. The smallpox serum is one of seventeen different serums now being produced in large quantities by the drug factory, which also produces ten kinds of tablets, seven kinds of tinctures and twenty kinds of Chinese compounds. The drug factory is constantly expanding its list of drugs and medicines and increasing its output to provide the four International Peace Hospitals of the Northwest with necessary supplies, many of which up to this time had to be smuggled through enemy lines. In Shensi, where the drug factory is located, the area is rich in medicinal herbs, and the factory's department of Chinese medicine is producing two hundred medicines based on native products. Many of the native herbs commonly used by herb doctors have been found to have the healing and corrective qualities claimed for them by these traditional medical men of China. In the department of western medicine, ampules for injection are prepared from imported raw materials at a saving of 60 per cent over the cost of foreign finished supplies. The third division, the manufacturing department, last year produced 5,000 pounds of absorbent cotton and 4,000 pounds of fine gauze. In addition to other products, 1,000 pounds of tinctures have been produced monthly. Sodium chloride, sodium sulfate and other sulfur products, much needed by the hospitals and mobile units, are now available. Besides preventive serums and life saving drugs, the drug factory is producing such products and by-products as cod liver oil, phenol solutions and medicinal soaps. Most of the medicines are being prepared in tablets, pills, powders, solutions and tinctures instead of the ancient and bulky form of aqueous extracts. A search for substitutes for imported drugs is being carried on in the laboratory, since one of the main problems of the Northwest has been and still is its inaccessibility because of blockades. Of the two hundred workers employed by the factory, China Aid Council reports that approximately one fourth are regularly instructed in chemistry, physics and pharmacology by the chemical engineers and the technical staff. All take part in management training, and the aim is the establishing of other such cooperative centers throughout the area. The most urgent problems to be met are lack of sufficient technicians, adequate machinery and funds for maintenance and training.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Nov. 28, 1942

London During a Year of Attacks from the Air

The report of the county of London medical officer of health and school medical officer for 1941, which has just been published, covers the second whole year of the war and for the first time gives a complete account of health conditions under the strain. During the heavy bombing of London in the first five months of 1941 the public health services were carried on under conditions of difficulty, but despite destruction of life and property they were never disorganized. No matter where the blow fell, new arrangements were speedily made and the work went on. When a hospital was partly or wholly put out of action, patients and staff were promptly transferred elsewhere. Temporary ambulance stations and school clinics appeared within a few days or hours after a loss. During the period of heavy air attacks the population of London fell considerably by evacuation. This, with the absence of any serious epidemics, made the reduced hospital accommodation quite sufficient. The practice of rapidly evacuating air raid casualties and other acutely ill patients from the London hospitals to others outside London was of great assistance in keeping beds available for casualties.

The aggregation of large numbers of persons in air raid shelters led to apprehension that epidemics would develop, but they did not. The number of deaths from all causes in 1941 was 43,537, against 57,459 in 1940. Diseases due to droplet infection might have been expected to increase, but the deaths from influenza, pneumonia and bronchitis were in each case less than in the previous year. Cerebrospinal fever also showed a reduction. It is remarkable that there were only 2 deaths from scarlet fever. In 1893 these numbered 1,415. Scarlet fever has now become a mild disease with a case mortality below 1 per thousand. There was some increase in diphtheria. According to the usual biennial cycle there should have been an epidemic of measles in the winter of 1939-1940, but dispersal or some other cause broke the rhythm and the deaths numbered only 29, compared with 235 in 1938. Whooping cough deaths increased from 10 in 1940 to 111. Typhoid caused only 17 deaths, and no case was attributable to infection by water, despite frequent disturbances of the drainage systems by bomb explosions. There was a definite decrease in the number of admissions to mental hospitals, as in the last war. Inspections of school children and comparison with the same age groups in the prewar years showed no evidence of mental or physical deterioration.

Medical Aid to Russia

Mrs. Churchill, president of the Red Cross Aid to Russia Fund, announces that despite many other demands on their charity the public has subscribed $10,000,000. On returning from his visit as head of a British medical mission to Moscow, Sir Charles Wilson, president of the Royal College of Physicians, brought back a tremendous list of needs. Among the articles dispatched were blankets, first aid pouches, children's clothes, 2 tons each of chloroform and ether, 10,000 Kg. of sulfanilamide, 50,000 Kg. of chloramine, 150,000 dissecting forceps, 77,000 hypodermic syringes, 200,000 ampules of strophanthin, 18,000 scalpels, 60,000 surgical scissors, 54,000 tourniquets, 523,000 yards of rubber sheeting, 100 portable x-ray sets, 30 tons of blood transfusion tubing and 30 tons of cocoa butter. For many of the articles special methods of production had to be introduced, and some instruments were manufactured for the first time in this country. The call for cocaine and procaine hydrochloride, which had to be and was met, was for quantities which equaled three years' normal use in Britain. In addition to medical supplies, at the request of the British government, 400,000 woolen garments were sent to Russian refugees restored to regained territory.

Women Medical Students

During the academic years 1940-1941, of the 5,265 students of medicine and dentistry in the University of London 11.7 per cent were women. Three fifths of these were at the London School of Medicine for Women. In the other schools only 5 per cent were women. In the remaining universities of Great Britain, of 7,687 students of medicine and dentistry 21.4 per cent were women. During the war the total number of students has only slightly diminished—from 13,636 in 1938-1939 to 12,952 in 1940-1941, and the number of women has only slightly increased—from 2,013 to 2,261. In a letter to the *Times*, Prof. A. V. Hill (physiologist and member of Parliament) states that medicine and dentistry are professions particularly suitable for women, especially in the coming important developments of public health services, maternity and child welfare, school medical and dental services and the women's services, and that many women are anxious to enter them but are rejected, particularly in London, not for any other reason than that they are women. The majority of the London schools refuse to accept them at all. If they took them in the same proportion as the provincial schools, there would now be five hundred more women students in London. Even the present shortage of manpower has not led the London schools to modify their policy. They have taken a large number of young men who had better be in the fighting services. Protesting against this position, Professor Hill suggests that the minister of labor should refuse to reserve any more men to begin the study of medicine in schools which do not accept women.

Medical Education in Municipal Hospitals

London already has twelve undergraduate medical schools as well as postgraduate schools. These are all attached to voluntary hospitals (so called because supported by voluntary subscriptions). But in recent years another important hospital system has arisen: the municipal hospitals, under the control of the London County Council, which are supported not by subscriptions but by taxes. They have no undergraduate medical schools attached to them, though they constitute the largest hospital system in the world, but they have already established an important postgraduate school. In a report submitted to the council by its general purposes committee the establishment of an undergraduate medical school is proposed. The report takes the form of the evidence given by the council to the interdepartmental committee on medical schools, recently set up by the minister of health. The new school would be set up at one of the council's larger general hospitals and would utilize other hospitals and schools as required. It would become an internal school of the University of London, which would provide the teaching staff, or alternatively the council itself would be responsible for the direction of the school. It is claimed that the experience which the council has gained in seven years of administration of the British Postgraduate School should be of great value in the new scheme. The new school, unlike the other London schools, would be open to women as well as to men.

The council's interest in medical education arises from its position as the major health authority of London and the largest civilian employer of medical staff in the country and from the facilities offered by its hospitals, which number one hundred. For some years it has provided for certain clinical teaching—in obstetrics, fevers, psychiatry, venereal diseases and others—by the affiliation of its hospitals with the voluntary ones. Up to the outbreak of war, eleven of the medical schools were

linked with sixteen of the council's "acute" general hospitals, in which classes and demonstrations were conducted by the council's medical staff. Teaching in obstetrics is already given at ten of the council's hospitals to students from nine London schools. Plans are in hand for the teaching of psychologic medicine after the war in the council's mental health services. It is suggested that the service performed by the field of public health and social welfare should be brought more closely to the notice of medical students as a means of teaching them the wider aspects of social and preventive medicine and that the council's schools can do this. Finally, the report calls for greater coordination of postgraduate medical education in London.

Arrangements for the Care of Children of War Workers

The large number of women engaged in war work, many of whom are married and have children, has created a new problem. To enable mothers with young children to undertake war work, about a thousand wartime nurseries have been established and five hundred more are in preparation. There are also four hundred special nursery classes for the children of war workers and nearly three hundred in preparation. In addition over a hundred thousand children under the age of 5 years are in ordinary elementary schools, and there are sixty-three nursery schools. But there are still many women whom industry wants for whose children there is no provision. The Ministry of Labor's solution is "child minder" schemes, which were brought forward some months ago, but few were started, as there was a prejudice against them from fear that the children would be neglected. However, they have been a success in Birmingham, where they are known as the Children's Home Service. They are based on child welfare centers, where the mother and the prospective "minder" are brought together. The latter has usually children of her own. The ministry pays her $1.50 a week for each child on condition that it is brought to the center when required, and the mother pays $2.50 and provides the rationed foods.

The Electroencephalogram in Criminal Trials

In 1929 Berger observed that electrodes applied to the normal scalp gave oscillations of potential of 10 per second on a recording instrument. This was subsequently confirmed by other observers. The oscillations are due to electrical activity of the cortical cells. It was subsequently shown that characteristic changes of rhythm occur in epileptic patients not only during the fits but between them. This fact has led to the electroencephalogram being used as evidence on the question of responsibility in criminal trials. A soldier who fired a rifle at a corporal pleaded that he had no knowledge of the affair and suffered a head injury a few hours previously. The attack was apparently without motive. An electroencephalogram showed abnormalities compatible with the head injury and he was discharged. In another case, in which a brutal and apparently purposeless murder was committed, the defense was that it was done in a period of postepileptic confusion. The evidence of epilepsy was tenuous but an abnormal electroencephalogram was produced. The medical witnesses said that an absolute diagnosis of epilepsy could not be made on this, as no subclinical attacks were seen, but it made the diagnosis likely. The man was found "guilty but insane" and so escaped capital punishment.

Fungi as Food

Before the war we imported two thirds of our food supply. The need to devote as much shipping as possible to the transport of munitions has reduced the amount of imported food to one third of our total supply, and the loss of the other third has been compensated by extension of our agriculture. We are looking to sources of food growing wild which are ordinarily neglected, such as the edible fungi. Dr. John Ramsbottom, keeper of botany in the Natural History Museum, South Kensington, has called attention to them in a letter to the *Times*. This has led to more than four hundred letters, often accompanied by specimens, being received at the museum, and evidence has been obtained on the eating of forty different kinds, though the general public knows and uses only two kinds. The museum is anxious to spread a knowledge of the best and most easily recognizable edible species. To this end an exhibit of fresh specimens of both edible and poisonous fungi, supplemented with colored plates, is on view. Moreover, lectures are being delivered on the subject. It is emphasized that the popular traditional tests as to what is edible and what is not are quite unreliable. Such, for example, is the belief that if a mushroom can be peeled it is edible. The deadly Amanita phalloides peels beautifully. Also the belief that all species which grow under trees are poisonous is wrong. If people would learn to recognize the best edible fungi and also the poisonous, a palatable food, such as is commonly eaten on the European continent, would be saved from going to waste.

Sailors Leave Their Sick Beds to Fight

The epic story of the greatest convoy ever sent to arctic Russia, which withstood a battle of four days, in which it was attacked by airplanes, surface vessels and submarines, has been told in the press. The principal medical officer stated that when the alarm sounded all the patients in the sick bay leaped from their beds to their action stations at the guns and, when the situation eased, returned to their beds. One of them who had some badly damaged ribs manned a gun forward. After the first attack he was asked by the medical officer how he felt. "Bit of a headache, sir; I could do with a couple of tablets," he replied.

Surveys of Hospital Services

As shown more than once previously in THE JOURNAL, the calm confidence with which the country regards the outcome of the war is proved by the various forms of planning for the future. The Ministry of Health is now carrying out its third survey of hospital services, which covers northeastern England. The survey is in the hands of the Nuffield Provincial Hospitals Fund, which was established as one form of the munificence of the automobile magnate Lord Nuffield. The trust has appointed Mr. H. L. Eason, chairman of the General Medical Council, Dr. Veitch Clark, late health officer of Manchester, and Mr. W. H. Harper, house governor of Wolerhampton Hospital, to carry out the survey. Other surveys are to follow until the whole country is covered. Mr. Ernest Brown, minister of health, has stated that the first object of the surveys is to see how far each patient can as easily as possible obtain the best treatment of the kind he needs.

New Uniform for Nurses

For the first time in over sixty years the nursing uniform of the London Hospital has been changed. The new dress became necessary because the old one took about 6 yards of material, and today war rationing allows only 4½ yards. The familiar large Victorian "leg of mutton" sleeve has given place to a small puff sleeve. Soft collars and cuffs stitched with mauve or blue to match the frock and made from apron material take the place of starched collars and the sisters' cuffs. There is a new hat with the hospital badge stitched on the hat band and new overcoat in place of the old "London" cloak. Aprons will be worn only by sisters and nurses when on ward duty. During the war the sisters will wear their yard long cap tails only on special occasions. The changes mean that 1,680 fewer aprons and 10,686 fewer detachable sleeves will be worn during the year.

BRAZIL

(From Our Regular Correspondent)

Oct. 31, 1942.

American Trypanosomiasis in Brazil

Oswaldo Cruz and Carlos Chagas described in 1909 a new human trypanosomiasis affecting some poor peasants in the state of Minas Gerais, Brazil. The parasite has been named Schizotrypanum cruzi, and the new disease has been known as Chagas' disease or American trypanosomiasis. Since then acute and chronic cases of the disease have been described in almost all the countries of the Western Hemisphere, with the principal exceptions of Canada and the United States. However, naturally infected vectors (blood sucking bugs of the family Reduvidae) have been found in the states of California, Texas and Arizona, and a bug of the state of Florida (Triatoma sanguisuga ambigua) was experimentally infected two years ago by A. Packchanian of the National Institute of Health. At the recent meeting of the eleventh Pan American Sanitary Conference, held in Rio de Janeiro, Dr. Carlos Chagas Jr. read a paper on the situation of American trypanosomiasis in Brazil. The evolution of the parasite in vertebrates (armadillo, opossum, dog, cat, guinea pig and rat) has recently been restudied and developed by Dias and Freitas, whose researches on the life cycle of S. cruzi have definitively established that, in the bug, the evolution takes place mainly in the posterior intestine, a fact of the greatest importance because it permits the normal transmission of the disease by the feces of the bug, full of the metacyclic forms of the trypanosome. After many negative results, some workers have succeeded in the transmission of the parasite through the bite of the insect, but this exceptional fact is explained by Dias as a consequence of the regurgitation of infective forms from the stomach. Dr. Carlos Chagas Jr. has established that the intracellular evolution lasts about five days. The initial focal proliferation of the trypanosomes has enabled Romaña, from Argentina, to raise the hypothesis of the entry of the parasites through the conjunctival membranes of the eye, a fact now considered well proved. The most recent studies have also demonstrated that Schizotrypanum has a great affinity for the reticuloendothelial system, and thus the protozoon is considered a primitive parasite of this system.

As S. cruzi cannot live in the exterior world through the direct transmission from bug to bug, because the insects are not naturally given to coprophagism and to cannibalism, nor is there hereditary transmission of the trypanosomes in the bugs, the presence of infected insects in any area is a sure indication of the existence of vertebrate reservoirs of the parasites. Out of the twenty states of Brazil, in thirteen the natural infection of reduviids has been proved. The most numerous examinations have been made in the state of Minas Gerais, where, up to the present, 3,855 insects have been found naturally infected out of a total of 12,336, or 31.3 per cent. In Brazil, more than thirty different species of reduviids have been found naturally infected, and several vertebrates have been found as reservoirs of the trypanosomes. Among the domestic animals acting as reservoirs, the dog and the cat are important, since they are so closely connected with the poor peasants in the adobe and other primitive houses infected by the bugs. Among the sylvatic reservoirs the most important are the armadillos (Dasypus novemcinctus, Dasypus hybridus and Euphractus sexcinctus), which harbor parasites with nuclear index identical to that of the trypanosomes from man.

The majority of the human cases of the American trypanosomiasis observed by Carlos Chagas were chronic cases, but in a few children he was able to recognize the acute form of the disease. The exact diagnosis was difficult, because it was necessary to base it on the finding of the trypanosomes in the peripheral blood, and the parasites are rather rare in this medium. The xenodiagnosis, carried out by allowing uninfected reduviids to suck the blood in the suggestive cases and later trying to ascertain the presence of the parasite in the bugs, became an important diagnostic tool, but it was somewhat difficult to use. Some progress had also been made by the use of the complement deviation test, as devised by Machado and Guerreiro of the Oswaldo Cruz Institute. Some years ago Mazza and Romaña described what is now commonly named the Romaña sign, i. e. the unilateral strong palpebral edema and conjunctivitis, with definite ganglial reaction, an important sign for the detection of acute cases. The cardiac form of the disease (the most common chronic clinical form) is characterized by a strong Machado-Guerreiro reaction and tachycardiac, bradycardiac, extrasystolic and arrhythmic symptoms. In no other disease is the myocardial process so intense as in the American trypanosomiasis. A striking fact is the finding of many cases of sudden death in small towns, in the areas affected by the disease. It is now well recognized that there is no connection between Chagas' disease and goiter, contrary to what Chagas himself emphasized in his early writings. In the state of Minas Gerais the geographic distribution of trypanosomiasis coincides with that of simple goiter, but in Argentina, for instance, these areas of prevalence of the two diseases are entirely different.

Dogs as Healthy Carriers of Brazilian Typhus

The São Paulo state strain of typhus fever was related in 1932 by cross immunization by Lemos Monteiro, by Parker and Davis and by Dyer of the United States to Rocky Mountain spotted fever. The state of Minas Gerais type of endemic typhus, first recognized in 1934 by J. A. Monteiro and Octavio Magalhães, was proved in 1939 to be identical with the spotted fever virus (THE JOURNAL, Jan. 10, 1942, p. 159). Thus there is only one strain of Brazilian typhus, and that one is identical with the United States spotted fever. Prof. Octavio Magalhães and Dr. Adyr Rocha of the University of Belo Horizonte, Minas Gerais, who have actively continued to work on the Brazilian typhus, profiting by several massive domiciliary foci of the disease, with 2, 4, 7, 9 and even 12 severe or slight cases in the same dwellings in rural areas around Belo Horizonte city. Their ideas about the epidemiology of the Brazilian disease are that it is quite different from the disease prevalent in the United States. They have insisted (*Brasil-med.* **49**:465 [May 25] 1935) that the Brazilian typhus has a different epidemiology, and among the particular epidemiologic features they have pointed to the importance of the dog as a carrier. They point to the fact that, since 1930, the dog has been shown to act as a healthy reservoir for the virus of the Mediterranean littoral typhus fever (fièvre boutonneuse). In this case the vector is a tick (Rhipicephalus sanguineus) which also transmits the disease hereditarily. Also Salles Gomes of São Paulo reported in 1933 that a tick (Amblyomma ovale), taken from a pet dog of a house where a few cases of Brazilian typhus had occurred, was infected, but no further significance was given to the fact. Magalhães showed that in Minas Gerais about 25 per cent of the patients had strictly domestic occupations, and many of them were young children. In September of last year Magalhães published a report of a small focus in a suburban house of Belo Horizonte, where, during the course of a few months, he recognized 1 severe and fatal case of typhus, 3 mild cases and 1 labeled "inapparent case," i. e. with no symptoms but presenting the virus in the blood. In 2 dogs and in several bedbugs (Cimex rotundatus) the presence of the virus has been recognized, and, what is more important, 1 of the dogs remained infective for forty days.

To investigate this subject fully, Magalhães and Rocha devised an extensive experimental study, the conclusions of which have been published in the *Brasil-medico* (**56**:370 [Aug. 1] 1942). They worked with 139 dogs from different places in the state

of Minas Gerais: 4 have been inoculated experimentally, and 135 were naturally infected. The Weil-Felix test has been done with OX 19, OX 2, OX L, and OX K strains, with the maximum results of 1:1,280 for the OX 19, and 1:640 for the other strains. The results of the Weil-Felix tests were as follows for the 135 cases of natural infection: 54 dogs from houses of the urban zone of Belo Horizonte, 79 per cent positive; 76 dogs from houses of the suburban zone, 90 per cent positive; 5 dogs from rural areas, 87 per cent positive. Three of the 4 inoculated dogs gave a positive Weil-Felix reaction. It was possible to try to recover the virus from only 31 dogs. The blood of the dogs has been injected into guinea pigs and into rhesus monkeys with 11 positive results, or 35.5 per cent. These studies emphasize the importance of pet dogs as natural carriers of Brazilian typhus, and the results are worth trying again in other places of the Americas, as the virus of Brazilian typhus is not different from that of Rocky Mountain spotted fever.

Primary Bronchial Diphtheria

A case of rare localization of diphtheria has been reported by Dr. Celestino Santos of the J. C. Rodrigues Hospital of Rio de Janeiro in a child 2 years old. The patient was feverish, seeming to have a simple cold. On the following day he became asphyxic, with a stridulous cough. The examination of the respiratory apparatus disclosed no abnormalities through percussion and auscultation. A careful examination of the throat, the tonsils and the uvula was also entirely negative except for a slight hyperemia. Early on the third day the state of the patient became still worse and another physician suspected diphtheria, injected 20,000 units of antitoxin, and sent the child to an otorhinolaryngologist, who could find nothing more. The examination of specimens taken from the throat and from the nose was negative. The patient was subjected to tracheotomy but died a few hours later. The necropsy disclosed an extensive diphtheric patch in the bronchi, beginning to invade the pulmonary parenchyma. This is an extremely rare localization of diphtheria difficult to diagnose.

Alcoholization of the Mesoappendix

As a result of observations on 407 patients operated on for appendicitis, in which the alcoholization of the mesoappendix was employed, Dr. Henrique Smith concluded that this new method is a means of obtaining a painless period after the operation. The alcoholization produces no complications for as long as three years after the operation, according to the observations of Dr. Smith. The method is being used by many Brazilian surgeons. It is not necessary to use more than 2 or 3 cc. of alcohol to obtain good alcoholization.

Inter-American Congress of Surgery

The first Inter-American Congress of Surgery will be held at Santiago, Chile, on November 14 with the cooperation of the surgical societies of Argentina, Brazil, Bolivia, Paraguay, Uruguay and Chile.

The treatment of acute peritonitis will be the principal theme of the discussions. Also to be discussed are the sequels of pyogenous pleuritis of nontuberculous origin and fractures of the humerus. This congress was organized to commemorate the centenary of the University of Chile.

Immunization Against Tuberculosis

According to the data just now published by the prefecture of Rio de Janeiro, there were registered in that city 33,082 births in 1941. Forty-four per cent of these children, or 14,582, were immunized against tuberculosis by BCG.

Sulfanilamide During Cesarean Section

In a recent paper read before the São Lucas Society, Dr. José Saldanha Faria reported the results from the use of sulfanilamide during cesarean section. He pointed out the benefits of this technic, saying a few words about intrauterine sulfanilamide when a cesarean section is necessary. He advocated the use of this medicament in the practice of gynecology and in myomectomies when the enucleation may accidentally open the uterine cavity.

Marriages

FURMAN TOWNSEND WALLACE, Chester, S. C., to Miss Virginia Records of Indianapolis in Charleston, S. C., August 29.

WILLIAM HERBERT PARSONS to Mrs. Victoria Blanchette Gaddy, both of Ellerbe, N. C., in Florence, S. C., July 20.

JOHN OVERBEY WATKINS to Mrs. Mary Leigh Johnstone, both of Spartansburg, S. C., in New Orleans, October 2.

DAVID E. BAGSHAW, Saginaw, Mich., to Mrs. Lena Helms Brittain of Atlanta, Ga., in Toronto, Ont., Canada, July 18.

CHARLES E. CLONINGER, Claremont, N. C., to Miss Alice Larkin of Coatopa, Ala., in Washington, D. C., recently.

GLENN CLARENCE WOLF, Naperville, Ill., to Miss Marianne Simonson of Dayton, Ohio, in Chicago, September 30.

CHARLES HOWARD EVANS JR., Rochester, Minn., to Miss Mary Jane Richholt of Holgate, Ohio, September 20.

ARCHIBALD C. RANDOLPH, Upperville, Va., to Mrs. Theodore Ayer Winthrope in Washington, D. C., September 3.

EDWARD R. BARBER, Clio, S. C., to Miss Eleanor Thompson of Salem, N. J., at Chicopee Falls, Mass., recently.

HENRY RUTHERFORD BUTLER JR., Atlanta, Ga., to Miss Rheba May Ashmore at Fort Huachuca, Ariz., October 9.

JOHN MCGILL PRATT, Hickory Grove, S. C., to Miss Dorcas Cromer at Carlisle Barracks, Pa., September 29.

BEVERLY TODD TOWERY, Bowling Green, Ky., to Miss Jane Ethel Raborg of Nashville, Tenn., September 3.

EDWIN MASON ROBERTSON, Durham, N. C., to Miss Eliza Isabelle Buckles of Bristol, Va., September 19.

REX DECKER HAMMOND to Miss Barbara Tyler, both of Chicago, in Little Rock, Ark., October 10.

HENRY PRICE DEYERLE, Harrisonburg, Va., to Miss Mary Elizabeth Savage at Franklin, August 25.

HERBERT WILLIAM BONDURANT JR. to Miss Ann Kennedy Irby, both of Atlanta, Ga., September 15.

HUBERT C. PATTERSON JR., Albemarle, N. C., to Miss Elizabeth R. Fox of Philadelphia, August 14.

ALLAN ESTES WALKER, Waxahachie, Texas, to Miss Erma Murphy at Ardmore, Okla., August 6.

CHARLES PETERSON MARVIN, St. Paul, to Miss Lucia Carole Bellinger of Atlanta, Ga., October 1.

IRVING I. COWAN, San Diego, Calif., to Miss Joan Clarice Reydman of Milwaukee, October 30.

EUGENE DANIEL GUYTON to Miss Eloise Bethea McCall, both of Marion, S. C., September 3.

FRANCIS X. MARINO, Springfield, Ill., to Miss Margery Bond in New Orleans, August 17.

LUTHER WARREN CHESNEY to Miss Marion Margaret Moore, both of Knoxville, Tenn., recently.

JOHN B. BIRCH, Maywood, Ill., to Miss Gladys Risley of Onarga at Watseka in September.

JOHN M. SLAUGHTER, Millersville, Ala., to Miss Molly Powell of Florence, September 7.

ISIDORE BRILL, Champaign, Ill., to Miss Rosa Lee Rose in Washington, D. C., October 13.

JOHN E. MOSS, Mobile, Ala., to Miss Eva Jean Williams of Charlotte, N. C., September 9.

THOMAS WORTH CROWELL, Seattle, to Miss Jean Shorkley of Carpinteria, Calif., recently.

ARTHUR DENTON JONES to Miss Mercy Lee Farris, both of Jacksonville, Fla., October 4.

RUDOLPH FINZER VOGT to Miss Catherine Clark Duffy, both of Louisville, Ky., recently.

RONALD E. CORKERN, Natchitoches, La., to Miss Ruby Jones at Franklinton recently.

LAWRENCE S. SIEGEL to Miss Sandra Coe, both of Los Angeles, November 8.

WILL W. STRANGE to Miss Charline Googe, both of Booneville, Miss., in July.

EDWIN B. BILCHICK to Miss Ruth Coleman, both of New York, July 30.

Deaths

Rossner Enders Graham ✠ Oakland, Calif.; Tulane University of Louisiana School of Medicine, New Orleans, 1914; Army Medical School, Washington, D. C., 1917; specialist certified by the American Board of Psychiatry and Neurology, Inc.; a first lieutenant in the medical reserve corps at Base Hospital, Fort Sam Houston, Texas, in 1916; commissioned a major in the medical corps of the U. S. Army in 1918; regimental surgeon with the 27th infantry, American Expeditionary Forces, in Siberia in 1919; chief of the neuropsychiatric service at the Letterman General Hospital, San Francisco, from 1919 to 1922; station surgeon and psychiatrist in the U. S. Disciplinary Barracks at Alcatraz in 1922; consultant at Mills College; in the neuropsychiatry service of the Oakland Health Center from 1923 to 1928; served on the staffs of the Peralta, Highland-Alameda County and Providence hospitals; aged 54; died, October 6.

William John Dougherty ✠ Brownsville, Texas; Bellevue Hospital Medical College, New York, 1898; member of the Medical Society of the State of New York and of the National Gastroenterological Association; specialist certified by the American Board of Psychiatry and Neurology, Inc.; also a lawyer; formerly on the surgical staff of St. Vincent's Hospital, New York, attending neurologist at the Broad Street Hospital, New York, and an assistant alienist in the psychopathic department at the Bellevue Hospital, New York; at one time on the staffs of St. John's Riverside and St. Joseph's hospitals, Yonkers, N. Y., and the U. S. Veterans Hospital, New York; in 1937 was appointed consultant psychiatrist for the Catholic Archdiocese of New York; aged 64; died, November 26, in the Mercy Hospital of chronic myocarditis.

Samuel Hanford McKee, Montreal, Que., Canada; McGill University Faculty of Medicine, Montreal, 1900; specialist certified by the American Board of Ophthalmology; formerly professor of ophthalmology at his alma mater; member and past president of the American Academy of Ophthalmology and Otolaryngology; member of the American Ophthalmological Society and the Association for Research in Ophthalmology, Inc.; formerly vice president of the Pan American Congress of Ophthalmology; past president and secretary of the Montreal Medico-Chirurgical Society; on the staff of the Montreal Maternity Hospital from 1906 to 1914; served with the Canadian Expeditionary Forces during World War I; on the staffs of the Montreal General and Alexandra hospitals; aged 67; died, November 25.

John Harold Morris ✠ New York; Cornell University Medical College, New York, 1914; specialist certified by the American Board of Surgery; assistant clinical professor of surgery at the New York University College of Medicine; formerly assistant professor of clinical surgery at the New York Post-Graduate Medical School, Columbia University; fellow of the American College of Surgeons; served as a major overseas with the New York Post Graduate Hospital unit during World War I; visiting surgeon at the Welfare Hospital for Chronic Diseases and St. Vincent's Hospital; associate visiting surgeon, Bellevue Hospital; assistant visiting surgeon, Willard Parker Hospital; aged 53; died, November 24, in the New York Hospital.

Frank W. Cregor ✠ Indianapolis; Medical College of Indiana, Indianapolis, 1894; retired as head of the department of dermatology and syphilology at the Indiana University School of Medicine in 1942; specialist certified by the American Board of Dermatology and Syphilology; member of the American Dermatological Association; member of the Judicial Council of the American Medical Association from 1923 to 1933 and member of the House of Delegates 1925-1926 and from 1929 to 1934; past president of the Indiana State Medical Association; formerly a member of the state board of health; at one time state senator; on the staffs of the Indianapolis City, Indiana University and Methodist hospitals; aged 69; died, Dec. 9, 1942.

George Skinner McCarty, Walla Walla, Wash.; University of Maryland School of Medicine, Baltimore, 1905; formerly a passed assistant surgeon in the U. S. Public Health Service Reserve and on the staff of the Veterans Hospital number 50, Whipple Barracks, Prescott, Ariz.; served with the American Expeditionary Forces in France during World War I; aged 60; served as a specialist in tuberculosis on the staff of the Veterans Administration Facility, where he died, November 19, of acute glomerular nephritis due to acute prostatitis with abscess and active pulmonary tuberculosis.

Joshua Allen, Philadelphia; Hahnemann Medical College of Philadelphia, 1878; aged 91; died, November 8.

Charles Arburn, Wadesville, Ind.; Kentucky School of Medicine, Louisville, 1889; member of the Indiana State Medical Association; aged 84; died, November 27, of hypostatic congestion of the lungs and chronic myocarditis.

Henry Bagully, Brooklyn; Long Island College Hospital, Brooklyn, 1900; member of the Medical Society of the State of New York; aged 74; died, September 25.

Stanley A. Baranowski, Milwaukee; Milwaukee Medical College, 1910; member of the State Medical Society of Wisconsin; chairman of the advisory board of the Johnston Emergency Hospital; a member of the staff of St. Luke's Hospital and a house physician at St. Joseph's Orphanage; aged 57; died, November 1, of acute cardiac dilatation and chronic myocarditis.

George H. Barbour, Helena, Mont.; Medical College of Ohio, Cincinnati, 1886; member of the Medical Association of Montana; member of the state board of medical examiners from 1899 to 1906; surgeon for the American Smelting and Refining Company for forty years; aged 79; died, November 19, in St. Peter's Hospital of chronic myocarditis.

Samuel S. Barrett, Nevada, Ohio; Western Reserve University Medical Department, Cleveland, 1895; aged 80; died, November 5.

Edward M. Bench ✠ Galena, Ill.; Northwestern University Medical School, Chicago, 1898; recently served on the draft board and during World War I; on the staff of the Mercy Hospital, Dubuque, Iowa; aged 70 died, November 27, of cerebral thrombosis.

William Bernard Burns, Boston; Maryland College of Eclectic Medicine and Surgery, Baltimore, 1914; aged 54; died, November 15, in Millis of coronary thrombosis.

Allen Melville Carpenter, Carmel, Calif.; Cooper Medical College, San Francisco, 1895; aged 72; died, November 18, in the Roosevelt Hospital, New York, of carcinoma of the colon and renal insufficiency.

James S. Cleland, Chicago; Missouri Medical College, St. Louis, 1898; aged 64; died, November 15, in the Veterans Administration Facility, Hines, of coronary heart disease and angina pectoris.

Bert Daniel Clutch, Booneville, Ark.; Kansas City (Mo.) College of Medicine and Surgery, 1919; aged 61; died, November 22, of a cerebral hemorrhage.

John Moore Crump, Oakland, Calif.; University of the City of New York Medical Department, New York, 1879; aged 88; died recently of congestive heart disease.

Frederick M. Eaton, Oakland, Calif.; Hahnemann Medical College and Hospital of Philadelphia, 1889; aged 80; died recently of chronic myocarditis.

John Ralph Ferguson, Monroe, La.; University of Nashville (Tenn.) Medical Department, 1908; aged 63; died, October 31.

Charles Webster Hamm ✠ Troy, N. Y.; Albany Medical College, 1893; past president and vice president of the Rensselaer County Medical Society; aged 73; died, October 3.

Baynard Lawton Harris, St. Charles, S. C.; University of Nashville (Tenn.) Medical Department, 1897; aged 69; died, November 5.

James Harris, Lakeland, Fla.; Cincinnati College of Medicine and Surgery, 1893; for two years taught pathology at his alma mater; aged 80; died, November 15, in the Morrell Memorial Hospital of senility, renal insufficiency and prostatic infection.

Cephas Cole Hill, Darlington, S. C.; University of Maryland School of Medicine, Baltimore, 1904; member of the South Carolina Medical Association; past president of the Tri-County Medical Association and of the Darlington County Medical Society; for many years surgeon for the Atlantic Coast Line and Seaboard railroads; recently served as a medical examiner for the draft board and in the same capacity during World War I; aged 64; died, November 8, in the McLeod Infirmary, Florence.

Charles Addison Hurd, Northwood, Iowa; State University of Iowa College of Medicine, Iowa City, 1888; member of the Iowa State Medical Society; for many years health officer, commissioner of insanity and coroner; a member of the Selective Service System during World War I; organized and for many years president of the Worth County Historical Society; aged 81; died, November 9.

Blyford B. Jackson, Lawrence, Kan.; Meharry Medical College, Nashville, Tenn., 1909; aged 64; died, November 7.

Egerton Sowerby Jackson, Bronxville, N. Y.; Trinity Medical College, Toronto, Ont., Canada, 1888; formerly assistant attending physician at the Bellevue Hospital, New York,

and clinical assistant at the New York Hospital, New York; aged 73; died recently of hemorrhage into the cerebrum, arteriosclerosis and cerebral endarteritis.

Hampar Boghoss Kazanjian, Los Angeles; Baltimore Medical College, 1898; member of the Massachusetts Medical Society; aged 68; died, September 20, of cerebral hemorrhage due to arteriosclerosis.

William Charles Keettel, Lyons, Neb.; John A. Creighton Medical College, Omaha, 1901; aged 67; died, November 12, in a hospital at Omaha of paralysis agitans and bronchopneumonia.

Marion Luther Klinefelter ✠ St. Louis; Washington University School of Medicine, St. Louis, 1903; member of the Clinical Orthopaedic Society and of the American Academy of Orthopaedic Surgeons; fellow of the American College of Surgeons; aged 69; consulting orthopedic surgeon, Frisco Employees' Hospital; orthopedic surgeon to the Evangelical Deaconess Home and Hospital and the Missouri Baptist Hospital, where he was shot and killed by a former patient, November 28.

Knute Andreas Kyvig, Poulsbo, Wash.; College of Physicians and Surgeons of San Francisco, 1905; aged 74; died, October 27.

John William MacMullen, South Mountain, Pa.; College of Physicians and Surgeons, Baltimore, 1904; member of the Medical Society of the State of Pennsylvania; served with the American Expeditionary Forces in France during World War I; chief of the state tuberculosis clinic at Harrisburg from 1907 to 1934; aged 63; since 1934 senior resident physician on the staff of the Pennsylvania State Sanatorium number 1, where he died, November 17, of cardiovascular disease.

Jerry James McFarland, Lebanon, Tenn.; Vanderbilt University School of Medicine, Nashville, 1893; member of the Tennessee State Medical Association; formerly bank president; aged 71; on the staff of the McFarland Hospital, where he died, November 11, of myocarditis and hypertrophy of the prostate.

William Rennie McKinnon, Detroit; University of Michigan Medical School, Ann Arbor, 1918; aged 57; on the staff of the Highland Park (Mich.) General Hospital, where he died, November 23, of cardiorenal vascular disease.

Arnold Edwards Mulford, Bridgehampton, N. Y.; University of Georgia Medical Department, Augusta, 1913; aged 56; died, October 26.

Deo Clifton Munger, Ellsworth, Wis.; Rush Medical College, Chicago, 1888; aged 79; died, October 24.

Henry H. Nast, Los Angeles; University of Denver Medical Department, 1897; aged 83; died, November 3, of coronary thrombosis and arteriosclerosis.

Norman Pearson, Pontiac, Ill.; Northwestern University Medical School, Chicago, 1901; aged 64; died, November 19, in a hospital at Peoria of bronchopneumonia.

John Joseph Price, Olyphant, Pa.; Baltimore Medical College, 1896; member of the Medical Society of the State of Pennsylvania; served during World War I; aged 68; died, October 28, in Wilkes-Barre.

Lucien Henry Arthur Ranger, Montreal, Que., Canada; Laval University Faculty of Medicine, Quebec, 1919; served during World War I; on the staff of the Hospital Ste. Jeanne d'Arc; aged 49; died, November 14.

Alexander H. Redding, Cedar Falls, N. C.; College of Physicians and Surgeons, Baltimore, 1887; member of the Medical Society of the State of North Carolina; aged 85; died, November 16, of heart disease.

Henry David Reed ✠ Pottstown, Pa.; Jefferson Medical College of Philadelphia, 1903; past president of the Montgomery County Medical Society; recently a member of draft board number 9; on the staff of the Pottstown Hospital; aged 62; died, November 17, of coronary occlusion.

Harry Campbell Reynolds ✠ Passaic, N. J.; New York Homeopathic Medical College and Hospital, New York, 1899; served in France as a major in the medical corps of the U. S. Army during World War I; fellow of the American College of Surgeons; recently became a director of the city's emergency hospital service, in charge of organizing medical and nursing units; aged 67; member of the board of governors and on the staff of the Passaic General Hospital, where he died, November 21, of pneumonia.

Peter Anthony Ritchie Jr., North Little Rock, Ark.; University of Arkansas School of Medicine, Little Rock, 1940; aged 27; died, November 10, in a hospital at Little Rock as the result of a fall when pushed from an automobile while trying to detain a drunken driver.

John Morrow Robb, Blind River, Ont., Canada; University of Toronto Faculty of Medicine, 1903; first elected to legislature of Ontario for constituency of Algoma in 1915; reelected in 1926 and in 1929; minister of health, province of Ontario, from 1930 to 1934 and minister of labor in 1934; built and equipped own private hospital at Blind River; aged 66; died, December 11.

Charles Henry Robbins, Altadena, Calif.; Baltimore Medical College, 1895; aged 73; died, September 9, of myocarditis due to chronic nephritis.

James F. Rupe, Smithville, Mo.; Ensworth Medical College, St. Joseph, 1886; member of the Missouri State Medical Association; aged 79; died, November 7, in the Trinity Lutheran Hospital, Kansas City, of uremia.

Charles Frederick Seafers, Palestine, Texas; Kentucky School of Medicine, Louisville, 1897; served as a medical examiner on the Jefferson County draft board during World War I; formerly member of the school board of Port Arthur; superintendent of St. Mary's Hospital, Gates Memorial, Port Arthur, from 1911 to 1917; aged 70; died, November 16, of coronary occlusion.

Eloise Augusta Sears, Boston; Boston University School of Medicine, 1888; aged 88; died, November 5.

Clarence Mars Selfridge, Oakland, Calif.; Hahnemann Medical College and Hospital of Philadelphia, 1887; aged 82; died, September 11, of bronchopneumonia.

Hirsh Hyman Shiell, Los Angeles; Detroit College of Medicine and Surgery, 1916; aged 53; died, November 9, of a cerebral vascular stroke due to hypertensive heart disease.

John Spicer, Goldsboro, N. C.; Bellevue Hospital Medical College, New York, 1889; aged 72; died, November 15, in Winston-Salem of pulmonary thrombosis.

Henry Storgaard, Seattle; Chicago Hospital College of Medicine, 1916; formerly assistant surgeon in the U. S. Public Health Service Reserve; assistant health officer of King County; aged 49; died, November 7.

Charles Mathias Tinsman, Adin, Calif.; College of Physicians and Surgeons, Keokuk, Iowa, 1898; at one time associated with the Indian Service; aged 76; died, November 6.

William Arthur Trevena, Ocoee, Tenn.; Atlanta (Ga.) School of Medicine, 1911; served as a member of the county court and of the county school board for many years; aged 61; died, November 14, in the Newell and Newell Sanitarium, Chattanooga, of intestinal obstruction following an old appendicitis operation.

Harry Abram Walker ✠ Somerville, Mass.; Cornell University Medical College, New York, 1905; served during World War I; on the staff of the Somerville Hospital; aged 61; died, October 30.

James Edward Wallace ✠ Biloxi, Miss.; Medical Department of Tulane University of Louisiana, New Orleans, 1909; served as a captain in the medical corps of the U. S. Army during World War I; on the staff of the New Biloxi Hospital; aged 62; died, October 28.

Harold Homer Webb ✠ Ottumwa, Iowa; University of Maryland School of Medicine, Baltimore, 1912; specialist certified by the American Board of Radiology, Inc.; member of the Radiological Society of North America, Inc., and the American College of Radiology; on the staffs of the Ottumwa Hospital, St. Joseph Hospital and the Sunnyslope Sanatorium; aged 52; died, November 4.

DIED WHILE IN MILITARY SERVICE

Cyrus Cathey Brown ✠ Medical Inspector, Commander, U. S. Navy, San Diego, Calif.; Johns Hopkins University School of Medicine, Baltimore, 1912; U. S. Naval Medical School, Washington, D. C., 1921; entered the medical corps of the U. S. Navy, Jan. 6, 1921; aged 56; died, November 9, at the Naval Air Station, Dutch Harbor, Alaska, of acute enteritic tuberculosis and hypernephroma of the right kidney.

John Richard Hatfield, Orlando, Fla.; University of Tennessee College of Medicine, Memphis, 1935; member of the Florida Medical Association; entered the Army of the United States as a first lieutenant Jan. 7, 1941 and was stationed at Fort Jackson, S. C., until May 5, 1942; was a major with the Johns Hopkins unit at the time of his death somewhere in the Pacific, October 22, of coronary thrombosis, aged 38.

Bureau of Investigation

STIPULATIONS

Agreements Between Federal Trade Commission and Promoters of Various Products

The following items are abstracts of stipulations in which promoters of "patent medicines," medical devices and cosmetics have cooperated with the Federal Trade Commission to the extent of agreeing to discontinue certain misrepresentations in their advertising. These stipulations differ from the "Cease and Desist Orders" of the Commission in that such orders definitely direct the discontinuance of misrepresentations. The abstracts that follow are presented primarily to illustrate the effects of the provisions of the Wheeler-Lea Amendment to the Federal Trade Commission Act on the promotion of such products.

Elip.—This preparation contained potassium bitartrate, sulfur and emodin, according to the Federal Trade Commission, with which agency Edmond W. Caforio, trading as Hempstead Selipon Company, Hempstead, N. Y., signed a stipulation in August 1942. In this Caforio agreed to discontinue the following misrepresentations: that "Elip" is a harmless remedy or cure for hemorrhoids or will dry them up, cause the suffering that attends hemorrhoids to cease, or relieve itching, inflammation or bleeding caused by this condition. Caforio further agreed to discontinue any advertisements which did not reveal that the product should not be used when the patient suffers from stomach ache, cramps, colic, nausea, vomiting or other symptoms of appendicitis; provided, however, that the advertisements need contain only the statement, "Caution: Use only as directed," when directions on the label include a warning to the same effect.

Girolamo Pagliano Syrup.—In a stipulation signed in August 1942 with the Federal Trade Commission, the Alpinol Corporation, New York, agreed to cease making these misrepresentations for their product: that it has a purifying effect on the blood or bodily humors, eliminates noxious substances, is a remedy or cure for any disease or possesses any therapeutic value except as a cathartic. Further, they agreed to discontinue any advertisements which did not clearly reveal that this syrup should not be used when abdominal pain, nausea, vomiting or other symptoms of appendicitis are present and that its frequent or continued use may result in dependence on laxatives; provided, however, that it would be sufficient for the advertisements to state, "Caution: Use only as directed," if the directions for use on the label contain a warning to the same effect.

Isidore Rosen, Distributor of Cosmetics of Various Manufacturers.—Under the name of Howard Wig Company, located in New York, Rosen sells hair goods, toilet preparations and related products, some of which are mentioned below. In October 1942 Rosen stipulated with the Federal Trade Commission that he would discontinue making the following misrepresentations: that healing will be accomplished by use of "Nadine Flesh Soap"; that "Nadinola Bleaching Cream" will clear away freckles or muddy, sallow skin or is capable of whitening the skin; that "High-Brown Cold Cream" is a skin food; that "Overtons High-Brown Bleach Ointment" is an effective treatment for pimples, blackheads, eczema or other skin diseases; that "Aida Hair Pomade" encourages the growth of hair or is a competent treatment for dandruff; that "High-Brown Hair Grower" will grow hair or be a competent treatment for dandruff; that "Apex Hair Preparation" is an effective treatment for dandruff or thin or falling hair or that "Apex Pomade" is an effective treatment for short, thin or falling hair, thin temples or scalp eruptions generally. Rosen further agreed to cease representing that "Mme. C. J. Walkers Hair Preparation," "Mme. C. J. Walkers Tetter Salve" and "Mme. C. J. Walkers Temple Grower" are hair growers or effective in promoting the growth of hair; that either "Overtons High-Brown Bleach Ointment" or "New Herolin Double Strength Skin Whitener" is an effective treatment for ringworm or indicated as an application for all cases of ringworm generally, unless in connection with such representation and in equally conspicuous type, it shall be made clear that the effectiveness of such application is limited to that of temporarily affording relief from the symptoms thereof.

Kitrab.—This was put out by one Anna Plotz, Chicago, and consisted of an iodine salve, according to the Federal Trade Commission, with which Miss Plotz signed a stipulation in August 1942. In this she agreed to cease representing that her product is a cure or competent treatment for scrofula or goiter generally, or any kind of goiter other than the simple type resulting from iodine deficiency. She further agreed to cease making representations which attribute to her product any action on goiter, scrofula or conditions similar to them, in excess of what it actually possesses.

Prunlax.—In September 1942 the Adams Laboratories, Inc., St. Louis, stipulated with the Federal Trade Commission that it would discontinue these misrepresentations in its advertising: that "Prunlax" is a remedy or cure for constipation, aids in toning up the liver or the kidneys or is effective in the treatment or prevention of backaches, headaches, biliousness, colds and swollen joints; that it renews or strengthens lost energy and keeps children full of energy, arrests colitis or the formation of hemorrhoids or fissures, or that prune juice is the basis of this preparation. The concern further stipulated that it would cease representing, through the use of the brand name "Prunlax" or with other words or pictorial representations, that its product derives its laxative properties from prunes, and agreed to stop using the word "Laboratories" in connection with its business when it does not own, control or direct a laboratory where research work is conducted in connection with manufacturing this nostrum. The concern further agreed to discontinue any advertisements which represented that Prunlax is safe to use or which failed to warn that it should not be used when abdominal pain, nausea or other symptoms of appendicitis are present and that the frequent and continued use thereof may result in dependence on laxatives. It was permitted, however, to limit these warnings to the statement, "Caution: Use only as directed," if the label contained directions for use which included this warning.

Red Hearts.—That this product would restore youthful vigor or sex vitality or act as an aphrodisiac or stimulant were misrepresentations which the Reese Chemical Company, Cleveland, agreed to discontinue, according to a stipulation which they signed with the Federal Trade Commission in August 1942. In March 1936 this concern was prosecuted and fined in a district federal court for violating the Pure Food and Drugs Act in selling two products, one of which was "Red Heart Blood Tabs," under false and fraudulent claims. In this connection government chemists reported that the "Blood Tabs" were pills coated with sugar and lime carbonate and containing chiefly an iron compound, small amounts of zinc phosphide, and plant extractives including nux vomica, capsicum and an emodin-bearing drug.

Speedo Headache Powders.—These are a product of the Standard Sales Company, Birmingham, Ala., which concern in October 1942 stipulated with the Federal Trade Commission that it would discontinue the following misrepresentations: that these powders will have any effect on colds in excess of such relief as they may afford for the pain and discomfort of head colds; that they will eliminate, remedy or cure head colds, minor muscular aches, simple neuralgia or jittery nerves, that they are a stimulant or contain special ingredients that dissolve in a hurry or that they are safe to use. The concern further agreed to discontinue any advertisements which did not clearly reveal that these powders should not be used in excess of the recommended dosage since such use might cause dependence on the drug, skin eruptions, mental derangement or collapse, and that they should not be taken by or administered to children. It was provided, however, that it would be sufficient for such advertisements simply to state, "Caution: Use only as directed," if and when a warning to the same effect appears with the directions on the labeling.

Sphinx's (Dr.) Sarsaparilla and Iron with Iodide Potash.—This nostrum was the subject of a stipulation signed with the Federal Trade Commission in September 1942 by C. E. Prescott, trading as Prescott Drug Company, Memphis, Tenn. In this he agreed to cease representing that his product is an effective treatment for bad blood, rheumatism, malaria, general run down condition or stomach trouble and cleanses the blood, liver and kidneys. He further agreed to cease representing by the use of the prefix "Dr." in the brand name that his product is made or offered for sale by a doctor of medicine, and to stop using the word "Sarsaparilla" to refer to any preparation which does not contain sarsaparilla in sufficient quantity to possess therapeutic value. Further, Prescott agreed to discontinue any advertisements which did not reveal that his preparation should not be used by persons suffering from tuberculosis or thyroid diseases or when abdominal pains, nausea or other symptoms of appendicitis are present; provided, however, that such advertisements need contain only the statement, "Caution: Use only as directed," if the directions for use on the label contain a warning to the same effect.

Sulfo-Bath.—That this gives relief from nervousness, colds, insomnia, eczema, hives or poison ivy, is "health-giving," provides radiant health, imparts energy, or has any effect on rheumatism, neuritis, sciatica, arthritis or lumbago, except to relieve their accompanying pains, were misrepresentations to be discontinued in the advertising, according to a stipulation which B. G. Pratt Company, New York, signed with the Federal Trade Commission in October 1942. This concern further agreed to cease representing that "Sulfo-Bath," by causing the skin to absorb sulfur, would give one a healthy or beautiful complexion or correct the conditions which cause dandruff, itching scalp, falling hair, skin troubles and severe cases of athlete's foot.

T-Lax.—This product was the subject of a stipulation made in September 1942 between the T-Lax Products Company, Birmingham, Ala., and the Federal Trade Commission. In this the concern agreed to cease representing that its product can be relied on to bring about or maintain good health; that it is effective in treating stomach, liver or kidney disorders, indigestion, biliousness or similar ailments; that it will act as a laxative or have any effect on the liver or act as a diuretic or aid to the kidneys; or that it will remove the poisonous accumulation from the blood stream or is different from all other products sold for the same purpose. The company further stipulated that it would discontinue any advertisements which represented that "T-Lax" is in all cases safe or harmless, or which did not warn that it should not be used when abdominal pains, nausea, vomiting or other symptoms of appendicitis are present; provided, however, that such advertisements need contain only the statement, "Caution: Use only as directed," when the same warning appears in the directions for use on the label.

Vaseline Hair Tonic.—In September 1942 the Chesebrough Manufacturing Company, Consolidated, and the McCann-Erickson, Inc., advertising agency, both of New York, stipulated with the Federal Trade Commission that they would cease representing that this preparation prevents or tends to prevent the recurrence of dandruff scales, affects the cause of dry scalp or goes to the root of that disorder.

Correspondence

THE FIRST CARDIAC CLINIC

To the Editor:—On Oct. 7, 1942 Mary E. Wadley died in Albany, N. Y., in the fulness of her 90 years. Her passing off the scene ought not to fail of being recorded. In the history of the development of interest in cardiac diseases Miss Wadley played an important even if not a conspicuous part. She was the first one to recognize the fact that cardiac patients were receiving less care than they deserve or than it was possible to give to them. Miss Wadley was head of the Social Service Department of the Bellevue Hospital in New York City. What she did was to create for the Bellevue Hospital Social Service a cardiac clinic for working adults. She saw the need and stimulated Dr. Hubert V. Guile to undertake the creation of the Friday evening clinic. The movement which she brought into being can most fittingly be described in her own words in a letter written by her on Feb. 9, 1938:

"It is quite true," she tells me, "that the initial move in establishing this clinic belongs to Bellevue Social Service. Scores of cardiacs discharged from the wards were referred to Social Service for convalescent care and for assistance in finding suitable employment. This we could do, but continued medical oversight was imperative if they were to carry on. For most of them this oversight was obtainable only in the day clinics, and day clinics and jobs were incompatible. The situation was most distressing to patients, to physicians and to the hospital. We social workers knew that the solution for a large proportion of cases could be found in a special evening clinic, but there was prejudice against evening clinics. Dr. Hubert Guile was deeply interested in these cases and he agreed to give his time to directing an evening clinic if the hospital authorities would consent to the innovation. They did consent to it as an experiment [A Survey of the Bellevue Experiment in Preventive Work for "Cardiacs," by Katharine Tyng, in *Bellevue and Allied Hospitals Social Service Reports*, 1910-1914, is available at the New York Academy of Medicine]. This was in 1911, and there has practically been no Friday evening at Bellevue since then without a Cardiac Clinic Session. We chose Friday for the clinic as that would give the patient a two day rest, if needed, with the loss of only half a working day, and he could be back on the job Monday morning before a new worker could replace him. Our Social Service Committee was greatly interested and contributed the salary of a full time special worker. After devoting his time for several years to this clinic, Dr. Guile felt he must retire. He had interested many young physicians in the opportunity the clinic afforded for an intensive study of heart disease. Dr. John Wyckoff had been one of the most interested assistants and he was persuaded to take Dr. Guile's place. He threw himself into the further development of the work with great zeal and was influential in the establishment of many similar evening clinics elsewhere."

In order to complete the record, it is desirable to quote the course of subsequent events:

"There is good evidence that with this account of the role played by the Social Service in this movement, Wyckoff would wholeheartedly have agreed. He insisted on designating this clinic 'Bellevue Hospital Social Service Cardiac Clinic for Working Adults,' for this was the title of the clinic when it was turned over to him in 1919 by Dr. Guile. In his plan of organization the Social Service was the center to which all action moved and to which all action returned. In 1925, when he described the organization of cardiac clinics to the Medical Society of the State of New York ["The first clinic in this country for ambulatory cardiacs was established in 1911 by Dr. Hubert V. Guile in Bellevue Hospital. It was begun because the Social Service Department of the Hospital felt that the number of returns of cardiac patients to the wards could be diminished if the patients could, on discharge, be cared for in a clinic less crowded than the General Medical Clinic, and manned by physicians who would have time to become interested in the special problems of the heart patient," *New York State J. Med.* **25**:996, 1925] the position of the Social Service at the center of things was conspicuously indicated. And he repeated these statements in 1929.

"'The first cardiac clinic in the United States as a matter of fact was organized at Bellevue Hospital in 1911 by Dr. H. V. Guile at the request of Miss Wadley, the head of the Social Service Department, who felt the pressing need for the medical supervision of the ambulatory cardiac. In 1919 I took over this clinic, having during the preceding eight years worked in it at various times' [A Consideration of Causes of Heart Disease from the Standpoint of a Social Worker, *Hosp. Social Service* **19**:514, 1929]" John Wyckoff, 1881-1937, by Alfred E. Cohn, *Bulletin of the Institute of the History of Medicine* **6**, No. 7 [July] 1938).

One of the pities in recording the lives of persons and the history of movements is frequently the paucity of information that is available. But in this instance by good chance the beginning is known of an important matter. The care of patients suffering from cardiac diseases moved, through Miss Wadley's insight and interest, into a new era. If there were cardiac clinics at all or cardiac clinics having a purpose such as this one before the one at Bellevue Hospital, it is unknown to us. And so both to record the beginning of a valuable movement as well as to commemorate the name of Mary E. Wadley, a distinguished worker in this vineyard of the Lord, it is gratifying to record this piece of history.

ALFRED E. COHN, M.D., New York.
Member, Rockefeller Institute for Medical Research;
Chairman, Committee on Research.

"WAR AND THE SPREAD OF EPIDEMIC DISEASES"

To the Editor:—No doubt you recall your editorial entitled "War and the Spread of Epidemic Diseases" in THE JOURNAL, Aug. 2, 1941, page 368. This was written in view of reports in regard to plague.

Because of certain recent positive findings of plague in rodents and their accompanying insects in Marin County, across the Bay from San Francisco, the question of reported plague was investigated. From the *Public Health Reports* of the United States Public Health Service for the last six months, April to October 1942, and the reports of the California State Board of Health, January to November 1942, plague has been demonstrated in rodents and their accompanying insects in twenty counties of California but not in San Francisco. Likewise it has been reported from the territory of Hawaii and the states of Montana, Nevada, Idaho and Oregon. Plague was demonstrated in these communities in fleas, lice and ticks and in tissue organs of ground squirrel, rat, pack rat, wood rat, brush rabbit, chipmunk and marmot.

This should demonstrate the magnitude of the problem of rodent plague, which happily is not being transmitted to human beings at the present time. The possibilities of transmission, however, from rodents and their accompanying insects in rural areas to the rodents and their accompanying insects, particularly rats and fleas, in cities has many dangerous angles.

J. C. GEIGER, M.D., San Francisco.
Director of Public Health.

EPIDEMIC KERATOCONJUNCTIVITIS

To the Editor:—Among some of the growing problems which have confronted both health officers and industrial physicians in the country during the past year has been that of epidemic keratoconjunctivitis, called by some "shipyard conjunctivitis." The disease is apparently new to this country, but it has appeared in epidemic form both on the West Coast and in the East (and perhaps elsewhere) during the short space of a few months. During this period, however, much has been learned, to which recent articles testify (Hogan, M. J., and Crawford, J. W.: Epidemic Keratoconjunctivitis, *War Med.* **2**:984 [Nov.] 1942. Sanders, Murray: Epidemic Keratoconjunctivitis, *Arch. Ophth.* **28**:581 [Oct.] 1942. Isolation of a Virus of Epidemic Keratoconjunctivitis, Current Comment, THE JOURNAL, Oct. 17, 1942, p. 538). This information is not general as yet and apparently epidemic situations can develop insidiously in factories before the nature of the conjunctivitis in its potential seriousness is recognized.

To my knowledge the disease is not reportable in this country, and because of this and other obvious reasons it seems wise to bring it to the attention of THE JOURNAL. It is earnestly requested that if new outbreaks, or suspected outbreaks, of this disease (epidemic keratoconjunctivitis) should occur, notification of this fact be made to Dr. Murray Sanders (Department of Bacteriology, College of Physicians and Surgeons, 630 West 168th Street, New York City).

Dr. Sanders has been assigned by the Board for the Investigation of Epidemic Diseases in the U. S. Army to study this problem and to assist in the control of this disease.

JOHN R. PAUL, M.D.
Director, Commission on Neurotropic Virus Diseases,
Board for the Investigation and Control of Influenza
and Other Epidemic Diseases in the Army.

THE RETAN TECHNIC OF SPINAL DRAINAGE

To the Editor:—The editorial on forced spinal drainage in acute poliomyelitis in THE JOURNAL, September 26, should be corrected in the part describing my technic. Your description is erroneous. It begins with the statement "Since then the suggested technic has been simplified by Retan, who reported equally beneficial effects on omitting the accompanying lumbar or cistern puncture." The treatment period is of five hours instead of eight. The suggested rate of injection of the hypotonic salt solution is 10 cc. per pound hourly, never giving over a liter an hour and reducing the rate of injection during the last two hours of treatment; also decreasing the rate of injection if the blood pressure rises. Free drainage of cerebrospinal fluid is never allowed for fear of cerebellar herniation. The technic in relation to drainage of cerebrospinal fluid follows: At one-half hour intervals the nurse in charge of the case should remove the stylet from the needle and allow 5 cc. of cerebrospinal fluid to drain if the fluid flows from the needle in a stream; if it flows in a rapid drop, she is to remove 2 cc.; if in a slow drop she is to replace the stylet in the needle without removing any fluid. It has been shown that the drainage of cerebrospinal fluid is not related to the therapeutic result. These small amounts of cerebrospinal fluid are removed to prevent possible increase in intracranial pressure.

GEORGE M. RETAN, M.D., Syracuse, N. Y.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

ANNUAL CONGRESS ON MEDICAL EDUCATION AND LICENSURE

CHICAGO, Feb. 15-16, 1943. Sec., Council on Medical Education and Hospitals, Dr. H. G. Weiskotten, 535 North Dearborn Street, Chicago.

BOARDS OF MEDICAL EXAMINERS
BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Examinations of boards of medical examiners and boards of examiners in the basic sciences were published in THE JOURNAL, Dec. 26, page 1422.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Parts I and II. Various centers, Jan. 20-22 and March 1-3. Part III. Chicago, Jan. 5-7. Exec. Sec., Mr. Everett S. Elwood, 225 S. Fifteenth St., Philadelphia.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Written. Part I.* Various centers, Feb. 13. Candidates in military service may take Part I at their place of duty. *Oral. Part II.* Pittsburgh, May 19-25. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh.

AMERICAN BOARD OF OPHTHALMOLOGY: *Oral.* June. Sec., Dr. John Green, 6830 Waterman Ave., St. Louis.

AMERICAN BOARD OF OTOLARYNGOLOGY: *Oral.* New York, May or June. Final date for filing application is March 1. Sec., Dr. Dean M. Lierle, 1500 Medical Arts Bldg., Omaha, Neb.

AMERICAN BOARD OF PEDIATRICS: Starting July 1, 1943, Group I will be abolished. Sec., Dr. C. A. Aldrich, 707 Fullerton Ave., Chicago.

AMERICAN BOARD OF PSYCHIATRY & NEUROLOGY: Detroit, prior to the meeting of the American Psychiatric Association. Final date for filing application is March 1. Sec., Dr. Walter Freeman, 1028 Connecticut Ave., N.W., Washington, D. C.

AMERICAN BOARD OF SURGERY: Part I. March 4. Final date for filing application is Jan. 25. Sec., Dr. J. Stewart Rodman, 225 S. Fifteenth St., Philadelphia.

AMERICAN BOARD OF UROLOGY: Chicago, Feb. 12-14. Sec., Dr. Gilbert J. Thomas, 1409 Willow St., Minneapolis.

Wyoming October Report

The Wyoming State Board of Medical Examiners reports the written examination for medical licensure held at Cheyenne, Oct. 5, 1942. Six candidates were examined, all of whom passed. The following schools were represented:

School	PASSED Year Grad.	Number Passed
University of California Medical School	(1929)	1
Johns Hopkins University School of Medicine	(1930)	1
St. Louis University School of Medicine	(1940)	1
Columbia University College of Physicians and Surgeons	(1939)	1
University of Oklahama School of Medicine	(1914)	1
Osteopath *		1

* Examined in surgery only.

New York Endorsement Report

The New York State Board of Medical Examiners reports 81 physicians licensed to practice medicine by endorsement from June 1 through July 26, 1942. The following schools were represented:

School	LICENSED BY ENDORSEMENT Year Grad.	Endorsement of
Leland Stanford Junior University School of Medicine	(1914)	California
University of Southern California College of Medicine	(1902)	California
University of Southern California School of Medicine	(1938)	California
George Washington University School of Medicine	(1929) (1940)	Penna., N. B. M. Ex.
Georgetown University School of Medicine	(1941, 2)	N. B. M. Ex.
University of Illinois College of Medicine	(1941)	N. B. M. Ex.
Johns Hopkins University School of Medicine	(1933) (1938), (1939)	N. B. M. Ex., Maryland
University of Maryland School of Medicine and College of Physicians and Surgeons	(1938), (1940, 2)	Maryland
Harvard Medical School	(1935), (1939), (1940)	N. B. M. Ex.
Tufts College Medical School	(1938)	N. B. M. Ex.
University of Michigan Medical School	(1925), (1939)	Michigan
University of Minnesota Medical School	(1932)	N. B.M. Ex.
Albany Medical College	(1939), (1940, 2), (1941, 4)	N. B. M. Ex.
Columbia University College of Physicians and Surgeons	(1938), (1939), (1940)	N. B. M. Ex.
Cornell University Medical College	(1939), (1940)	N. B. M. Ex.
Long Island College of Medicine	(1939, 2), (1941)	N. B. M. Ex.
New York Medical College Flower and Fifth Avenue Hospitals	(1937), (1940, 4), (1941, 3)	N. B. M. Ex.
New York University College of Medicine	(1939, 2), (1941, 2)	N. B. M. Ex.
Syracuse University College of Medicine	(1940), (1941)	N. B. M. Ex.
University of Buffalo School of Medicine	(1939), (1940, 3), (1941, 9)	N. B. M. Ex.
University of Rochester School of Medicine and Dentistry	(1940)	N. B. M. Ex.

Duke University School of Medicine.....(1939)N. B. M. Ex.
University of Cincinnati College of Medicine.....(1939)N. B. M. Ex.
University of Oregon Medical School.....(1937) Oregon
Hahnemann Medical College and Hospital of Phila..(1934) Penna.
Jefferson Medical College of Philadelphia.....(1916) W. Virginia
Temple University School of Medicine.....(1936)N. B. M. Ex.
University of Pennsylvania School of Medicine.....(1927) Penna., (1933) Louisiana
Woman's Medical College of Pennsylvania.....(1907) Penna.
University of Vermont College of Medicine.....(1940)N. B. M. Ex.
Medical College of Virginia.....(1940) Virginia
Karl-Franzens-Universität Medizinische Fakultät, Graz.(1938)N. B. M. Ex.
Medizinische Fakultät der Universität Wien.....(1926)N. B. M. Ex.
Université de Paris Faculté de Médecine.....(1936), (1940)N. B. M. Ex.
American University of Bierut School of Medicine....(1941), (1942)N. B. M. Ex.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Autopsies: Right of Employer's Insurance Carrier to Require Autopsy on Body of Employee.—Simpkins had been employed by the Jones Construction Company, but prior to actually assuming the duties of employment he died of a heart attack. Following the death, the defendant, the insurance carrier of the employer, with the permission of the industrial commission of South Carolina, had an autopsy performed on the body. Subsequently the plaintiff, the deceased's wife, sued the insurance carrier to recover damages for the performance of the autopsy. She alleged that she had neither filed nor intended to file a claim under the workmen's compensation act and that the autopsy was performed against her will and with no notice to her or any hearing whatever. The defendant demurred on two grounds: (1) that the plaintiff was not the proper party to maintain the suit, and (2) that the autopsy was authorized by the workmen's compensation act of South Carolina. The trial court overruled the first ground of demurrer but sustained the second ground, and the plaintiff appealed to the Supreme Court of South Carolina. The Supreme Court adopted in toto the opinion of the trial court, and it was published as the opinion of the Supreme Court.

With respect to the first ground for demurrer the trial court held that, in the absence of testamentary disposition, the surviving spouse if living with the decedent at the time of death is the proper party to maintain an action based on the mutilation of a corpse. If there is no surviving spouse, the court said, then the next of kin would be the proper party to maintain such a suit. But here the plaintiff, being the surviving wife of the deceased, is the proper person to maintain the action, and the first ground of demurrer interposed by the defendant was overruled.

As to the second ground of demurrer, the widow argued first that the fact that the deceased had not actually commenced work under his contract of employment precluded the application to this case of section 27 of the workmen's compensation act which provides that the employer, or the industrial commission, shall have the right in the case of death to require an autopsy. The court concluded, however, that that provision was applicable and that the mere fact of a hiring or of a contract for employment makes it applicable even though there had been no assumption of the duties of employment by the employee. The widow next argued, in effect, that the workmen's compensation act was inapplicable as granting authority for an autopsy because she had neither filed any claim under the act nor intended to file any. The act, however, said the court, does not require an employer to wait until the claimant has filed with the commission a written claim for compensation before making his demand for a physical examination of the claimant. Such requirement would defeat the purpose of such examination. The employer is entitled to know the condition of the claimant at the time of the injury. He may take steps to minimize the effects of the injury and thus reduce his liability. To say that the claimant may delay the physical examination for so long a time after the injury as he wishes is to put it in his power to defeat the benefit to the employer of such examination. Accordingly, continued the court, the filing of a claim or the indication of the filing of a claim has no bearing on the operation of the act. The widow then argued that the autopsy was performed at the instance of the insurance carrier rather than of the employer. In answer the court pointed out that an insurer certainly stands in the shoes of its insured employer, having his rights and being subject to his obligations.

The widow contended that since the deceased died as the result of a heart attack, not as the result of an industrial accident, the right to an autopsy conferred by the act on the employer or on the industrial commission did not apply. We cannot, said the court, impose the restriction on the act contended for. The language of the act is plain and unambiguous. The act confers the right to an autopsy "in any case of death" of an employee. There is no specification as to the nature of the deaths to which the autopsy right applies. It was undoubtedly realized in the enactment of this law that there are and always will be deaths to employees which present a borderline between accidental and natural origins.

In the complaint the widow alleged that she had objected to and refused to consent to the autopsy; that she was not given an opportunity to be heard by any judicial or quasi judicial body; that there was no hearing by such body or as required by law, and that the autopsy was had by a request, without notice to her, to the secretary of the industrial commission, without a hearing before the commission or an order of the commission therefor. These facts, she claimed, indicated a high handed, illegal and unlawful autopsy in violation of her rights. But, said the court, the provision in question provides: "The employer . . . *shall* have the right . . . to require an autopsy." It does not state "may"; it does not qualify; it is unequivocally mandatory. There are no provisions relating to notice, consent or objections. The statute specifically provides that "the employer, or the Industrial Commission" shall have the right to require the autopsy. There is no ambiguity. We are not at liberty to insert any requirements as to consent or notice, regardless of whether or not we think such requirements advisable. Accordingly the court held, in effect, that because of the provisions of the workmen's compensation act the insurer had a right to require an autopsy and that an autopsy so performed was not in contravention to any rights of the widow. The judgment in favor of the insurance company was affirmed.—*Simpkins v. Lumbermens Mutual Casualty Co., 20 S. E. (2d) 733 (S. C., 1942).*

Society Proceedings

COMING MEETINGS

Annual Congress on Industrial Health, Chicago, Jan. 11-13. Dr. Carl M. Peterson, 535 North Dearborn St., Chicago, Secretary.

Annual Congress on Medical Education and Licensure, Chicago, Feb. 15-16. Dr. H. G. Weiskotten, 535 North Dearborn St., Secretary.

American Academy of Orthopaedic Surgeons, Chicago, Jan. 17-21. Dr. Myron O. Henry, 825 Nicollet Ave., Minneapolis, Acting Secretary.

Annual Forum on Allergy, Cleveland, Jan. 9-10. Dr. Jonathan Forman, 956 Bryden Road, Columbus, Ohio.

Clinical Orthopaedic Society, Chicago, Jan. 18-21. Dr. Myron O. Henry, 825 Nicollet Ave., Minneapolis, Secretary.

Eastern Section, American Laryngological, Rhinological and Otological Society, Hartford, Conn., Jan. 15. Dr. Edward J. Whalen, 750 Main St., Hartford, Conn., Chairman.

Middle Section, American Laryngological, Rhinological and Otological Society, Detroit, Jan. 20. Dr. Voss Harrell, 2539 Woodward Ave., Detroit, Chairman.

Southern Section, American Laryngological, Rhinological and Otological Society, Chattanooga, Tenn., Jan. 28. Dr. Francis B. Blackmar, 1301 Broadway, Columbus, Ohio, Chairman.

Western Section, American Laryngological, Rhinological and Otological Society, Portland, Ore., Jan. 31. Dr. Irving M. Lupton, 1020 S.W. Taylor St., Portland, Ore., Chairman.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1932 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American J. Obstetrics and Gynecology, St. Louis

44:553-742 (Oct.) 1942. **Partial Index**

Utopian Obstetrics: Plan Promoting Efficiency to the Obstetrician and Service to the Patient. R. A. Bartholomew, Atlanta, Ga.—p. 553.
Detailed Technic of Modified Local Anesthesia for Cesarean Section. A. C. Beck, Brooklyn.—p. 558.
*Etiologic and Pathologic Factors in Series of 1,741 Fibromyomas of Uterus. R. Torpin, E. Pund and W. J. Peeples, Augusta, Ga.—p. 569.
Anencephalus (with Acute Hydramnios) Diagnosed by X-Ray. W. R. Payne and H. G. Bland, Newport News, Va.—p. 593.
*Changes in Female Genital Tract During Puerperium Induced by Sex Hormone Therapy. R. N. Rutherford, Seattle.—p. 595.
Clinical Experiments in Relation to Excretion of Estrogens: II. Functional Flowing; Urinary Estrogens Before, During and After Progestertone, Estriol and Cyclic Administration of Progesterone and Estradiol Benzoate. G. Van S. Smith, O. W. Smith and Sara Schiller, Brookline, Mass.—p. 606.
Glomerular Filtration and Renal Blood Flow in Hypertensive Woman and in Post-Toxemic Hypertension. C. E. Robinson, L. V. Dill, J. F. Cadden and C. E. Isenhour, New York.—p. 616.
*Spontaneous Abortion and Its Treatment with Progesterone. L. W. Mason, Denver.—p. 630.
Uses and Abuses of Radiation Therapy in Obstetrics and Gynecology. H. F. Traut, New York.—p. 638.
Nutrition Study in Pregnancy: Food Habits of 514 Pregnant Women. P. F. Williams and Florence G. Fralin, Philadelphia.—p. 647.
Sexual Libido in the Female. R. B. Greenblatt, F. Mortara and R. Torpin, Augusta, Ga.—p. 658.
Electroencephalogram in Pregnancy. F. A. Gibbs and D. E. Reid, Boston.—p. 672.
Convulsions Following Intravenous Administration of Pituitary Extract. C. L. Sullivan and R. J. Heffernan, Boston.—p. 675.
Treatment of Pelvic Inflammatory Disease with Intradermal Administration of Bacillus Coli Vaccine: Supplementary Report. E. G. Krieg, Detroit.—p. 681.
Estrogen Withdrawal Bleeding: Study of Comparative Activity of Various Estrogens. S. D. Soule, St. Louis.—p. 684.
Colostrum Test for Pregnancy in Prenatal Clinic. M. Pulver and L. B. Posner, New York.—p. 690.
Artificial Pyrexia in Four Pregnant Women. W. F. Mengert and W. D. Paul, Iowa City.—p. 702.
Allergic Shock Caused by Synapoidin. E. W. Phillips, Phoenix, Ariz. —p. 706.

Fibromyomas of Uterus.—Of the 1,741 fibromyomas that Torpin and his colleagues report on, 575 were in white and 1,166 in Negro women from 17 to 76 years of age. In the majority of the patients the tumors were multiple. In 301 white women the tumors were smaller than 5 cm. in diameter, and 197 had tumors larger than 5 cm.; 302 Negro women had tumors smaller than 5 cm. while in 586 they were larger. Not only were the Negro women affected three and one-third times as often as white women, but they also had one and a half times the incidence of the larger tumors. As regards pelvic infection, 93 of the 575 white women had salpingitis, while it was present in 633 Negro women, that is in 54 per cent of the 1,166. Forty per cent of all patients operated on for chronic salpingitis had fibromyomas. In the 575 white women 67 follicular and 43 luteal cysts were found; among the Negro women there were 225 follicular and 117 luteal cysts. Adenomyosis occurred in 21 white and in 18 Negro women. Necrosis was found in 45 white and in 190 Negro women. The incidence of necrosis was not greater in the earlier reports when operations were deferred longer than in recent years. Likewise, calcification was more frequent in the Negro women. Pure myomas were found in 11 white and in 37 Negro patients. In addition to the follicular and corpus luteum cysts there were 11 cystadenomas in the white patients; in 3 they were malignant. Twelve such cysts, 5 of which were malignant, occurred in the Negro women. Dermoid cysts of the ovaries occurred in nearly 1 per cent of the white patients (5 cases) and in 2⅓ per cent of the Negro women (26 cases). A comparison of the endometrial changes in 100 fibromyomatous uteri and in 100 nonfibromyomatous uteri revealed that 20 per cent of the fibromyomatous uteri in white women and 10 per cent of those in Negro women were hyperplastic. For the nonfibromyomatous uteri (removed for chronic salpingitis or for bleeding late in the reproductive life associated with chronic cervicitis) the respective figures were about 15 and 20 per cent. This definitely indicates that there is no special association of endometrial hyperplasia with fibromyomas.

Changes in Female Genital Tract.—The changes in three groups of 12 patients (normal postpartum puerperas, normal postpartum women given 10 mg. of diethylstilbestrol for twelve days and normal postpartum women given 10 mg. of methyl testosterone for twelve days) were studied by Rutherford by endometrial biopsy and vaginal smear. The endometriums and vaginal smears of the patients treated with the synthetic preparations demonstrated definite variations from the normal processes of involution, repair and regeneration. Involution was delayed by the diethylstilbestrol but not by methyl testosterone, but repair was hastened by the one and definitely retarded by the other. Regeneration, that is, covering of the surface epithelium, was hastened by the diethylstilbestrol but stromal regeneration was delayed. The methyl testosterone delayed regeneration. The effects of diethylstilbestrol were no longer present after one week and the effects of methyl testosterone three weeks after their withdrawal.

Spontaneous Abortion.—Mason discusses the nineteen abortions that occurred among three hundred and eleven consecutive pregnancies cared for by him in private practice. Six of the abortions occurred in 2 patients, who had three each. This incidence of 6 per cent is considerably less than is generally reported. All the women were in comfortable circumstances, usually reported early for antepartum care, had adequate diets and received thyroid or iodine if it was indicated by a basal metabolism test or the history, and foci of infection were cared for as soon as possible. If 50 to 80 per cent of abortions are pathologic and if the chief cause is defective germ plasm, somatic factors should play no part. However, if the maternal environment is a major etiologic factor a comfortable life and preventive treatment ought to make considerable difference. The low abortion rate in the present series, together with an apparent considerable success in the treatment of abortion in these women, would seem to lend confirmatory evidence to the latter view. Among the series of pregnancies, thirty-four "threatened" abortions were treated. In 30, or 82 per cent, the abortion did not occur and the patients were carried to term. Four aborted in spite of treatment, but 1 of these went to term in her next pregnancy; prophylactic treatment was begun shortly after the first missed menstrual period. The other 3 of the 4 were lost sight of. In addition there were 17 patients who were treated prophylactically from the beginning of their pregnancies. These patients gave a history of having had one to three previous consecutive abortions. Of these 17 patients, 15 were carried to term the first time such prophylactic treatment was given. All gave birth to normal babies, who continued to develop normally thereafter. The two failures are represented by the 2 patients who figured in six of the total nineteen abortions. In addition to all other measures which constitute good antepartum care, the only other agent used in the treatment was progesterone (proluton). Morphine was not used. The progesterone was given in 5 mg. doses (intramuscularly in oil) to patients with threatened abortion. If the symptoms were slight, this dose was given once a day; but, if the symptoms were more severe, 5 mg. was given twice a day for several days. When cramps and/or bleeding ceased the progesterone was not discontinued immediately, but the 5 mg. dose was usually given every other day for several days. The dose was then reduced to 2 mg. and continued for a week or more; then the intervals were lengthened and the injections were continued for perhaps two more weeks. Patients with a history of recurrent abortion were given progesterone therapy as soon as pregnancy was diagnosed. The patient with a history of two previous abortions and no successful pregnancy should be treated through the seventh month of pregnancy.

Am. J. Roentgenol. & Rad. Therapy, Springfield, Ill.

48:425-570 (Oct.) 1942

Roentgen Diagnosis and Treatment of Primary Pulmonary Neoplasm. G. W. Holmes, Boston.—p. 425.
Lymphosarcoma, with Special Reference to Reticulum Cell Type. E. L. Jenkinson, R. E. Kinzer and W. H. Brown, Chicago.—p. 433.
Value of Roentgen Therapeutic Test Dose in Differential Diagnosis of Mediastinal Tumors. L. Reynolds and T. Leucutia, Detroit.—p. 440.
*Roentgen Therapy of Pituitary Adenomas. H. D. Kerr and W. K. Cooper, Iowa City.—p. 467.
Radiation Treatment of Cerebellar Medulloblastoma: Report of Thirty-One Cases. E. P. Pendergrass, P. J. Hodes and E. W. Godfrey, Philadelphia.—p. 476.
Low Back Pain Resulting from Arthritis and Subluxations of Apophysial Joints and Fractures of Articular Facets of Lumbar Spine. W. G. Scott, St. Louis.—p. 491.
Spontaneous Pneumomediastinum (Mediastinal Emphysema). D. S. Kellog, El Paso, Texas.—p. 510.
*Patella Cubiti: Report of Four Cases. J. E. Habbe, Milwaukee.—p. 513.
Problem of "Tubal Sphincter" and of Intramural Portion of Fallopian Tube. P. Schneider, New York.—p. 527.

Roentgen Therapy of Pituitary Adenoma.—Kerr and Cooper have observed 25 patients from a year to ten years or until death after they were given roentgen therapy for their pituitary adenoma. The results in 14 of the 25 are considered excellent, good in 5 and poor in 6. Twenty-two of the 25 were given irradiation alone and 2 who first received roentgen therapy and failed to benefit were later found to have cystic tumors. The poor response of these 2 demonstrates the inadequacy of roentgen therapy for this type of tumor. The chief criteria for judging progression or regression of the disease are the visual field changes and loss of headache. Success or failure must be judged not on survivals but on preservation or restoration of vision and the general well-being of the patient. Irradiation appears to do this, especially if relatively heavy doses are employed. However, if the disease progresses during three to four months after roentgen therapy, surgical exploration should be carried out because the tumor is likely to be cystic. The relatively large doses employed by the authors resulted in untoward effects only once. The patient had arteriosclerosis and hypertension, and mental deterioration developed. These changes they attribute to the effects of irradiation on arteriosclerotic cerebral vessels associated with hypertension.

Patella Cubiti.—Habbe reports 4 cases of patella cubiti, each of which occurred as a unilateral abnormality. In the third case trauma was the chief if not the only etiologic factor; the abnormality, in a patient aged 15, was found about five weeks after trauma. This condition was followed for six months, when a relatively mature state of patella cubiti was present. In the first case there was a definite history of trauma to the right elbow when the patient was 14; the only recalled diagnosis was that of "fracture." It was supposed that an avulsion of the olecranon epiphysis occurred together with periosteal stripping on the proximal diaphysis of the shaft by the mechanism of muscle pull, which was then followed by closure of the epiphysis and new bone formation along the distal projection. The minor trauma which occurred at 22 brought the patella cubiti to light and had no bearing on the development of the bony abnormality and apparently none on the immediate or subsequent functional status of the elbow joint. The second and fourth cases are similar as regards the history of a childhood trauma occurring at or about the time the olecranon epiphysis begins to ossify. However, the fourth patient had a relatively satisfactory clinical recovery without benefit of examination or treatment. While an etiologic relationship between childhood trauma and the formation of the patella was obtainable, there may still be some doubt as to trauma being the only etiologic factor. The similarity of the so-called epiphysitis in other regions, from the standpoint both of normal growth of these secondary epiphyses and of their roentgen appearance in the presence of a growth disturbance, is emphasized. In true patella cubiti any traumatic factor to be significant in the development of the condition must occur in childhood or adolescence. Hence trauma occurring in an adult employee who shows such an abnormality is not a causative factor in its appearance, and the misinterpretation of "fracture" or "pathologic fracture" should not be made.

Archives of Ophthalmology, Chicago

28:767-958 (Nov.) 1942

Nature, Scope and Significance of Aniseikonia. W. B. Lancaster, Hanover, N. H.—p. 767.
Eye Dominance: Its Nature and Treatment. I. S. Wile, New York.—p. 780.
Neuropsychiatric Geriatrics. H. W. Woltman, Rochester, Minn.—p. 791.
Simple Posterior Sclerotomy and Sclerectomy: Adjunct to Operations for Glaucoma. S. A. Fox, New York.—p. 802.
Modification of Dickey Operation for Ptosis. S. R. Gifford and I. Puntenney, Chicago.—p. 814.
Cyclic Oculomotor Paralysis (Spasmus Mobilis Oculomotorius). O. Lowenstein and I. Givner, New York.—p. 821.
Binocular Vision: Normal and Abnormal. H. Werner, Northville, Mich.—p. 834.
Use-Abuse Theory of Changes in Refraction versus Biologic Theory. E. V. L. Brown, Chicago.—p. 845.
Color Discrimination in Industry. J. Tiffin, Lafayette, Ind., and H. S. Kuhn, Hammond, Ind.—p. 851.
Ancient Medical Jurisprudence, with Special Reference to Eye. B. L. Gordon, Atlantic City, N. J.—p. 860.
Transplantation of Superior Oblique Muscle for Oculomotor Nerve Paralysis. S. R. Gifford, Chicago.—p. 882.
*Retinopathy in Juvenile Diabetes Mellitus. F. J. Bloch, New York.—p. 891.
Particles of Steel Within Globe of Eye: Cause, Diagnosis, Prevention, Technic of Removal and Results. F. D. Gulliver, New York.—p. 896.
Irregular and Multiple Homonymous Visual Field Defects. M. B. Bender and I. S. Wechsler, New York.—p. 904.
Recent Contributions to Localization of Vision in Central Nervous System. Marion Hines, Baltimore.—p. 913.

Retinopathy in Juvenile Diabetes.—Bloch reports 2 cases of retinal changes in juvenile diabetes in which there was no renal pathologic change or abnormal blood pressure. A number of cases in the literature suggest that diabetes itself may produce the disease known as diabetic retinitis or diabetic retinopathy. The author believes that the controversial question as to whether diabetic retinopathy proper or the retinal changes are secondary to hypertension or arteriosclerosis can be decided on the following three bases: Clinical observation will show that there is a difference between the decided changes in the fundus in diabetes, in arteriosclerosis and in hypertension, especially with reference to the optic nerve and the macular region. Study at necropsy of the pathologic changes in eyes from persons known to have had diabetes may reveal that the retinal changes developed independently (Koyanagi). Also information will be obtained from study of the retinal changes in diabetic persons, especially young patients, whose renal and blood vascular systems are normal. Many of the previous case reports are valueless because description is lacking.

Archives of Pathology, Chicago

34:791-936 (Nov.) 1942

Spontaneous Coccidioidal Granuloma in Lungs of Wild Rodents. L. L. Ashburn and C. W. Emmons, Bethesda, Md.
Reduction of Pulmonary Resistance to Infection by Circulating Toxins. D. H. Sprunt and W. Camalier Jr., Durham, N. C.—p. 801.
Elastic Tissue: I. Description of Method for Isolation of Elastic Tissue. G. M. Hass, New York.—p. 807.
Heart Weight: I. Weight of Normal Human Heart. Pearl M. Zeek, Cincinnati.—p. 820.
Papillary Cystadenoma Lymphomatosum. M. Lederer and D. M. Grayzel, Brooklyn.—p. 833.
Pancreodochocholecystostomy and Experimental Production of Gallstones. H. G. Aronson, Chicago.—p. 843.
*Sudden Death Following Injection of Foreign Protein. B. M. Vance and G. Strassmann, New York.—p. 849.
Bilateral Cortical Necrosis of Kidney: Report of Two Cases. W. H. Sheldon and A. T. Hertig, Boston.—p. 866.
Relationship of Heart Size to Cholesterol Content in Experimental Atheromatosis of Rabbit. M. Hurwitz and L. Friedberg, Chicago.—p. 875.
Experimental Studies in Cardiovascular Pathology: VI. Pectin Atheromatosis and Thesaurosis in Rabbits and in Dogs. W. C. Hueper, New York.—p. 883.
Effects of Radiation on Normal Tissues. S. Warren, Boston.—p. 917.

Death from Foreign Protein.—Vance and Strassmann found in the office of the chief medical examiner of the city of New York reports of 7 instances of sudden death following injection of foreign protein. They have correlated these cases with 19 similar cases reported in the literature in which necropsies were also made. Five of the seven sudden deaths were of persons presumably nonasthmatic. They died after injections of antitoxin. The other 2 were known to have bronchial asthma; they died after injections of foreign protein. At

necropsy there were pronounced inflation of the lungs and signs of asphyxia due to bronchial spasm in all the patients. The brain of 2 was edematous and under compression. In 2 there was edema of the submucous layer of the upper portion of the larynx. Microscopic study of 6 demonstrated varying numbers of eosinophilic leukocytes in the bronchial wall, suggesting that the reactions were hypersensitive in nature. Of the 19 patients who were the subjects of the reports in the literature 13 were presumably nonasthmatic and 6 were known to have asthma. Six of the 18 nonasthmatic patients had received injections of antitoxin or some other foreign protein from six to fourteen days to a number of years prior to the one causing death. The remaining 12 had received only the one injection. The product injected immediately preceding the onset of the fatal symptoms was some derivative of horse serum in 17 and a typhoid vaccine in 1. It appeared that the greater the amount of protein administered the more rapid was the fatal reaction. Ten patients, 7 of whom were children, had difficulty in breathing soon after the injection and died within ten minutes. Death was due to asphyxia caused by muscular spasm of the smaller bronchi. The death of 4 occurred in twenty to seventy minutes; the symptoms began soon after the injection or after twenty to thirty minutes. The symptoms were asthmatic in type, and the lungs at necropsy were inflated. Four patients lived for several hours after the fatal injection of horse serum. Four of the 8 asthmatic patients received horse serum derivatives, 2 pollen extract, 1 a mixture of silkworm, sheep's wool and kapok and 1 guinea pig serum. Six of these patients had not received any previous injections of protein and 2 had had regular injections of pollen extract. The symptoms at the time of death were typical of an asthmatic attack, and at necropsy the lungs were inflated. The duration of the clinical course in these 8 cases varied from five to forty-five minutes.

Arkansas Medical Society Journal, Fort Smith

39:129-156 (Nov.) 1942

Importance of Spas in Military and Defense Program. W. S. McClellan, Saratoga Springs, N. Y.—p. 129.
Arteriosclerotic Heart Disease. J. N. Compton, Little Rock.—p. 136.

Bulletin of Johns Hopkins Hospital, Baltimore

71:191-252 (Oct.) 1942

Successful Construction of an Extrathoracic Esophagus. J. S. Davis and E. S. Stafford, Baltimore.—p. 191.
Comparative Activity of Sulfonamides Against Coliform Bacteria in Intestines of Mice. H. J. White, Baltimore.—p. 213.
Myocardial Necrosis in Rats on Potassium Low Diet Prevented by Thiamine Deficiency. R. H. Follis Jr., Baltimore.—p. 235.
Note on Absence of Syphilitic Reagin and Antigenic Substance in Urine. V. Scott, Baltimore.—p. 242.

Bulletin of Los Angeles Neurological Society

7:107-156 (Sept.) 1942

Cranial Injuries of the Pre-Columbian Incas with Comments on Their Mechanism, Effects and Lethality. C. B. Courville, Los Angeles, and K. H. Abbott.—p. 107.
Quadrilateral Space of Marie. J. M. Nielsen and A. P. Friedman, Los Angeles.—p. 131.
Hemorrhages into Lateral Basal Ganglionic Region: Their Relationship to Recovery from Cerebral Apoplexy. C. B. Courville and A. P. Friedman, Los Angeles.—p. 137.

California and Western Medicine, San Francisco

57:227-282 (Oct.) 1942

Objectives of Institutes on Wartime Industrial Health. R. T. Legge, Berkeley.—p. 233.
Industrial Hygiene in War Production. J. J. Bloomfield, Washington, D. C.—p. 233.
Industry's Manpower: Its Conservation. C. P. McCord, Detroit.—p. 237.
San Francisco Management Looks at Industrial Health. F. P. Foisie, San Francisco.—p. 238.
Los Angeles Management Looks at Industrial Health. V. R. Nabors, Los Angeles.—p. 239.
San Diego Management Looks at Industrial Health. W. F. Persons, San Diego.—p. 241.
Physicians' Legal Responsibilities in Industrial Medicine. C. H. Fry, San Francisco.—p. 242.
Problems in Industrial Surgery. N. J. Howard, San Francisco.—p. 242.
Industrial Injuries: Their Surgical Management. B. M. Frees, Los Angeles.—p. 243.

Cancer Research, Baltimore

2:739-810 (Nov.) 1942

B Vitamins in Cancerous Tissues: I. Riboflavin. M. A. Pollack, A. Taylor, Jean Taylor and R. J. Williams, Austin, Texas.—p. 739.
Id.: II. Nicotinic Acid. A. Taylor, M. A. Pollack, Margaret Jane Hofer and R. J. Williams, Austin, Texas.—p. 744.
Id.: III. Biotin. M. A. Pollack, A. Taylor, Alethea Woods, R. C. Thompson and R. J. Williams, Austin, Texas.—p. 748.
Id.: IV. Pantothenic Acid. A. Taylor, M. A. Pollack, Margaret Jane Hofer and R. J. Williams, Austin, Texas.—p. 752.
Possible Types of Mammary Gland Tumors in Mice. J. J. Bittner, Bar Harbor, Maine.—p. 755.
Morphology and Development of Testicular Tumors in Mice of a Strain Receiving Estrogens. C. W. Hooker and C. A. Pfeiffer, New Haven, Conn.—p. 759.
Relation of Diet to Development of Gastric Lesions in Rat. K. Sugiura, New York.—p. 770.
Studies on Rous Sarcoma Cells Cultivated in Vitro: I. Cellular Composition of Pure Cultures of Rous Sarcoma Cells. L. Doljanski and E. Tenenbaum, Jerusalem, Palestine.—p. 776.
Further Experiments on Extraction of Carcinogenic Factor from Human Cancerous Tissues. J. F. Menke, San Francisco.—p. 786.
Effect of α-Estradiol-3-Benzoate on Response of CHI Mice to 20-Methylcholanthrene. A. Segaloff, Detroit.—p. 794.
Phospholipids of Tumor Cells and Nuclei. Frances L. Haven and Sylvia R. Levy, Rochester, N. Y.—p. 797.

Connecticut State Medical Journal, Hartford

6:839-910 (Nov.) 1942

*Prevalence of Sporotrichosis in Connecticut: Review of Three Cases and Report of New Case. E. C. Weise, Bridgeport.—p. 841.
Physical Therapy in Medical Practice. F. H. Krusen, Rochester, Minn.—p. 848.
Medical Social Work, One of Many Resources Available to the Physician. Edith M. Baker, Washington, D. C.—p. 853.
The Antisocial Child. J. M. Cunningham, Hartford.—p. 856.
Cyclic Changes in Human Vaginal Epithelium: Preliminary Report. L. Newton, Bridgeport.—p. 862.
Chemical Casualties. H. W. Haggard, New Haven.—p. 864.

Prevalence of Sporotrichosis.—Weise reports his third case of sporotrichosis, the fourth to occur in Connecticut. The disease may be mistaken for syphilis, as the ulceronodular and gummatous lesions may bear a close similarity to cutaneous gummas. Certain types of cutaneous tuberculosis and, at times, low grade streptococcic lymphangitis may be imitated. The general practitioner should consider it as a possible diagnosis in obscure ulcerative, ulceronodular and gummatous conditions, particularly when the lymph nodes appear to be involved. Cultures from areas which have broken through the skin either will not reveal the fungus or they will be grossly contaminated with staphylococci and other organisms. Pure cultures can almost invariably be obtained by utilizing previously unopened lesions. The 3 other culturally proved cases of sporotrichosis which have occurred in Connecticut are reviewed. The physician should familiarize himself with the various manifestations of the disease so that its true incidence may be ascertained and its otherwise prolonged period of disability avoided by appropriate management.

Florida Medical Association Journal, Jacksonville

29:153-196 (Oct.) 1942

Burns, Various Types; Treatment and Prognosis from Military as Well as Civilian Viewpoint. R. S. Widmeyer, Jacksonville.—p. 165.
Endocrinology and Metabolism: Excerpts from Current Studies in Endocrinology and Metabolism. A. J. Bieker, St. Petersburg.—p. 169.
Management of Duodenal Ulcer. J. E. Maines Jr., Gainesville.—p. 171.
Treatment of Bacillus Pyocyaneus Infection of Cornea with Sulfonamides. H. D. Solomon, St. Petersburg.—p. 174.
Abnormal Electrocardiograms. M. S. Saslaw, Coral Gables, and K. A. Brewer, Oklahoma City.—p. 175.

Georgia Medical Association Journal, Atlanta

31:381-408 (Oct.) 1942

New Syndrome of Nocturnal Frequency Due to Endocrine Imbalance. R. B. Greenblatt, Augusta.—p. 381.
Incidence and Management of Carcinoma of Prostate Gland. E. G. Ballenger and H. P. McDonald, Atlanta.—p. 383.
Crawford Williamson Long (1815-1878). T. J. Collier, Atlanta.—p. 387.
Primary Pneumococcic Peritonitis: Report of Case. W. W. Baxley, Macon.—p. 392.
Periarteritis Nodosa: Report of Case Diagnosed Ante Mortem. B. P. Wolff, Atlanta.—p. 394.

Illinois Medical Journal, Chicago

82:241-324 (Oct.) 1942

Surgery of Biliary Tract. V. S. Counseller, Rochester, Minn.—p. 257.
Improved Methods in Diagnosis and Treatment of Protozoan Infections of Intestine. A. A. Knight, Chicago.—p. 263.
Observations on Psychosomatic Treatment of Peptic Ulcer in Women. D. W. Propst, Chicago.—p. 267.
Health Planning. J. H. Beard, Urbana.—p. 269.
Engines of the Body. F. G. Norbury, Jacksonville.—p. 274.
Comments on Allergy. R. G. Mills, Decatur.—p. 278.
Male Climacteric. C. H. Boswell, Rockford.—p. 280.
Prize for Good Health: Extending 4-H Principles to Adolescent Youth. M. L. Blatt, Chicago.—p. 282.
Some Visual Problems in Modern Industry. H. S. Kuhn, Hammond, Ind.—p. 286.
Graduate Education in Neuropsychiatry: Proposal for Chicago Plan. R. R. Grinker, Chicago.—p. 289.
*Treatment of Hereditary Glaucoma. W. G. Ackerman and T. D. Allen, Chicago.—p. 295.
Subdural Hematoma. P. C. Bucy, Chicago.—p. 300.
Differential Diagnosis and Surgical Care of Jaundiced Patients. C. B. Puestow, Chicago.—p. 311.

Treatment of Hereditary Glaucoma.—Ackerman and Allen diagnosed hereditary glaucoma in 6 of 14 descendants of the originally affected member representing three generations. The average age at onset of all 7 affected members was 11.6 years with a span from 7 to 15 years. There was no tendency to anticipation. There was difficulty in controlling the condition with miotics and surgery. A single goniotomy was effective in controlling the tension in four eyes. Two goniotomies were required to control the tension in three eyes, and in an eighth eye an iridencleisis was finally required to control the tension after five goniotomies, two cyclodialyses and a deep root iridectomy failed. From the results in the 7 cases it appeared that although miotics by themselves were relatively ineffective in controlling the tention before surgery they may aid to maintain the lowered tension following surgery. The finding of glaucoma at an early age is an indication to search for a tendency to glaucoma in every other member of the family so that it can be treated before much vision is lost.

Journal of Aviation Medicine, St. Paul

13:161-232 (Sept.) 1942

Indoctrination of Flying Personnel in Physiologic Effects of High Altitude Flying and Need for and Use of Oxygen. L. D. Carson, Washington, D. C.—p. 162.
*Erythrocytes and Hemoglobin Values in Acclimatization Produced by Discontinuous Anoxia. J. C. Stickney and E. J. Van Liere, Morgantown, W. Va.—p. 170.
Studies on Effects of Adding Carbon Dioxide to Oxygen Enriched Atmospheres in Low Pressure Chambers: II. Oxygen and Carbon Dioxide Tensions of Cerebral Blood. H. Himwich, J. Fazekas, H. Herrlich, A. E. Johnson, Albany, N. Y., and A. L. Barach, New York.—p. 177.
Influence of Certain Antimalarials and Related Agents on Lethal Effects of Anoxia. E. J. Van Liere and G. A. Emerson, Morgantown, W. Va.—p. 182.
Effect of Preoxygenation on Newborn Rats Exposed to Simulated Altitude of 55,000 Feet (Barometric Pressure of 67.8 mm. Hg): Preliminary Report. A. L. Barach, N. Molomut and S. Landy, New York.—p. 190.
Color and Composition of Light in Relation to Blackout. C. E. Ferree and G. Rand, Baltimore.—p. 193.
Color and Color Perception. A. J. Herbolsheimer, Washington, D. C.—p. 201.
Clinical Test for Dark Adaptation. V. P. Flynn, Pasadena, Calif.—p. 216.
Observations on Pilots of Eastern Air Lines. H. K. Edwards, Miami, Fla.—p. 219.

Erythrocytes and Hemoglobin Values and Acclimatization to Discontinuous Anoxia.—Aviators are subjected to discontinuous anoxia, as they spend but relatively short periods aloft. Stickney and Van Liere tried to determine in dogs how long it would take for distinctive signs of acclimatization to develop in an animal subjected to a given degree of anoxia for a certain period each day. The dogs were placed daily (except on Sunday) in a low pressure chamber in which various altitudes were simulated. Hemoglobin and erythrocyte determinations were usually made every week. At or after the third week the hemoglobin values rose, subsequently rising more or less uniformly until discontinuous exposure to anoxia was terminated. A distinct increase in the erythrocyte count did not occur before the fifth week, and thereafter it was practically uniform throughout the six months of discontinuous anoxia. Following the period of the anoxia the hemoglobin and erythrocyte values decreased uniformly to the original values in about eight to nine weeks, respectively. The original levels were attained as though there had been an overshooting of the mark. The plotting of the color index shows that the hemoglobin values tended to increase faster than the erythrocyte values until exposure to the simulated 18,000 feet had well begun, when there was a greater gain in erythrocytes. This was indicated by the reduction in the color index. This reversal was fairly constant throughout the rest of the anoxia period, and before the values returned to normal the color index tended to be even lower before it finally regained its initial value. The erythrocyte count was increased 84 per cent by the end of the sixteenth week after exposure to a simulated altitude of 18,000 feet. Acclimatization apparently does follow discontinuous exposure to anoxia, the degree being directly proportionate to the severity of the anoxia and the length of exposure.

Journal of Bone and Joint Surgery, Boston

24:739-1012 (Oct.) 1942. **Partial Index**

*Wounds in Modern War. J. A. MacFarlane, Toronto, Canada.—p. 739.
Primary Genetic Dysplasia of Hip With and Without Classic Dislocation. V. L. Hart, Minneapolis.—p. 753.
Repair of Complete Acromioclavicular Dislocation, Utilizing Short Head of Biceps. L. Vargas, Rio de Janeiro, Brazil.—p. 772.
Spastic Scoliosis and Obliquity of Pelvis. S. L. Haas, San Francisco.—p. 774.
*Influence of Sodium-Beta-Glycerol-Phosphate on Healing of Experimental Fractures. L. Sperling, W. D. Armstrong and S. Litow, Minneapolis.—p. 781.
*Immersion Foot. D. R. Webster, F. M. Woolhouse and J. L. Johnston, Halifax, N. S., Canada.—p. 785.
Localized Fibrocystic Disease of Bone: Results of Treatment in 152 Cases. R. H. Alldredge, New Orleans.—p. 795.
Arthroplasty for Congenital Dislocation of Hip: Late Follow-Up Report. P. C. Colonna, Philadelphia.—p. 812.
Etiology of Aseptic Necrosis of Head of Femur After Transcervical Fracture. E. L. Compere, Chicago, and G. Wallace, Rochester, Minn.—p. 831.
Obturator Sign as Earliest Roentgenographic Sign in Diagnosis of Septic Arthritis and Tuberculosis of Hip. H. W. Hefke and V. C. Turner, Milwaukee.—p. 857.
Contributory Clinical Observations on Infantile Paralysis and Their Therapeutic Implications. A. Steindler, Iowa City.—p. 912.
Local Application of Sulfonamides to Synovial Surfaces. E. M. Bick and H. C. Pheasant, Red Bank, N. J.—p. 937.

Wounds of Modern Warfare.—MacFarlane declares that for the wounds of modern mobile warfare it is of the greatest importance to evacuate the wounded by air or, failing this, to bring early surgery to the patient; that is, mobile medical units. The closed plaster treatment permits safe transportation over long distances without the necessity of changing dressings. Patients who had débridement and plaster fixation travel well and look fit on arrival. Furthermore, continued closed plaster treatment at the base hospital seems to be the method of choice. In Canadian hospitals the method is to be adopted as routine treatment. Experience in England and in Libya shows that war wounds should not be sutured. Sulfanilamide as a prophylactic measure is not sufficient to prevent gas gangrene and other infection in the contaminated wound. The author knows of no prophylactic against gas-forming organisms other than early removal of devitalized muscle. With débridement and local chemotherapy he has not seen increased healing or lessening of infection as compared to similar surgical treatment without chemotherapy. On the other hand, sulfonamides given by mouth after injury may decrease the incidence of severe streptococcic infection, particularly when there is delay in reaching an organized operating center. The application of sulfonamides to superficial wounds, particularly burns, is of undoubted value, but their routine use in deep penetrating wounds does not lessen the urgency for surgical treatment.

Sodium-Beta-Glycerol-Phosphate for Healing Fracture.—Sperling and his associates investigated the effect of intravenous injections of sodium-beta-glycerol-phosphate on the rate that fresh experimental fractures in rabbits healed. Twenty-seven animals received six to fourteen daily injections, by ear vein, of 0.1 Gm. of the drug in 4 cc. of solution. Twenty-two control animals with similar fractures were given injections of isotonic solution of sodium chloride. All rabbits were killed the day following the last injection. Roentgenograms of the limbs were taken before and after soft tissue was removed from them; they revealed an increase in callus about the fracture site

in the group treated with sodium-beta-glycerol-phosphate. Also the callus was more firm to palpation than that of the control animals. Healing appeared to have progressed further than in the control animals, the callus was larger, the fracture defect was more nearly bridged over and much more callus was adherent to the periosteum.

Immersion Foot.—Webster and his associates have observed 142 cases of "immersion foot," a condition produced by long immersion of the feet in cold water. As the condition may occur in feet exposed for long periods in subtropical waters, it cannot be classed as true frostbite. Almost all of the cases were the result of enemy action in the North Atlantic. The feet when the patients were removed from the open lifeboats or rafts on which they had been for varying periods were cold, swollen and waxy white, with scattered cyanotic areas. The patients complained that their feet felt heavy, "woody" and numb. The feet were anesthetic to pain, touch and temperature. Soon after the patients were removed from their craft the swelling increased rapidly, the feet became red, hyperemic and hot without sweating, and the pulse in the vessels of the feet was full and bounding. The initial anesthesia and hypesthesia were replaced by intense paresthesia on the eighth to the tenth day after removal from the traumatizing agent. A trial of treating the feet by dry refrigeration was made at Camp Hill Hospital, Halifax, N. S. With the feet elevated, dry cooling and refrigeration were achieved by the application of ice bags (changed every four hours), dry cooling by exposure to a fan and dry cooling at room temperature. A few hours after the ice bags were applied the patients were completely comfortable, the edema subsided and blebs filled with straw-colored fluid and those filled with extravasated blood were resorbed without breaking. The blebs refilled if cooling was discontinued prematurely. The 127 patients with minimal, mild and moderate involvement, with 1 exception, recovered completely after superficial desquamation over the entire foot and reeducation necessitated by an abnormal gait. Their average hospital stay was thirty and four-tenths days. Of the 15 patients with severe involvement 7 have been discharged after the loss of small areas of superficial tissue, which healed rapidly and did not require grafting. Of the 8 still confined to the hospital, 5 have gross tissue defects across the mid-dorsum of both feet, in 2 the superficial skin over the distal aspect of both feet has become mummified but is being shed and replaced by healthy tissue with epithelial islands throughout and in 1, to whose feet ice bags were applied for four weeks, the tissues of the feet had a healthy pink color, but in eight hours at room temperature a large quantity of blood was extravasated into the subcutaneous tissues. The feet became greenish gray, and a sharp line of demarcation between healthy and damaged tissue encircled the midtarsal region of both feet and tissue breakdown occurred. This will probably progress ultimately to extensive tissue loss over the distal aspect of both feet. The rationale of the treatment rested on the presumption that if the metabolic demands of the part could be reduced until the edema subsided, the extravasated blood resorbed and the vasomotor tone reestablished the tissue damage would be greatly ameliorated. Strict asepsis is essential because if infection develops in the damaged tissue the process spreads rapidly through all layers of the feet.

Journal of Experimental Medicine, New York

76:317-400 (Oct.) 1942

Effects of Excess Dietary Cystic Acid, *dl*-Methionine and Taurine on Rat Liver. D. P. Earle Jr., Katharine Smull and J. Victor, New York.—p. 317.

Studies on Eastern Equine Encephalomyelitis: VI. Facilitation of Infection in Mouse. L. S. King, New Haven, Conn.—p. 325.

Formation of Antibodies in Popliteal Lymph Node in Rabbits. W. E. Ehrich and T. N. Harris, Philadelphia.—p. 335.

Simultaneous Renal and Hepatic Excretion of Water, Cyanol and Azofuchsin I in Rabbits. W. E. Ehrich, Philadelphia.—p. 349.

Induced Resistance of Central Nervous System to Experimental Infection with Equine Encephalomyelitis Virus: I. Neutralizing Antibody in Central Nervous System in Relation to Cerebral Resistance. Isabel M. Morgan, R. W. Schlesinger and P. K. Olitsky, New York.—p. 357.

Control of Renal Excretion of Water: I. Effect of Variations in State of Hydration on Water Excretion in Dogs with Diabetes Insipidus. J. A. Shannon, New York.—p. 371.

Id.: II. Rate of Liberation of Posterior Pituitary Antidiuretic Hormone in Dog. J. A. Shannon, New York.—p. 387.

Journal of Investigative Dermatology, Baltimore

5:207-282 (Oct.) 1942

Relationship Between Certain Physicochemical Changes in Cornified Layer and Endogenous Bacterial Flora of Skin. L. Arnold, Chicago.—p. 207.

Studies in Abnormal Human Sensitivity to Light: II. Light Sensitivity in Prurigo Aestivalis, Eczema Solare and Urticaria Photogenica: Report of Experiments. S. Epstein, Marshfield, Wis.—p. 225.

Studies of Transmissibility of Syphilis: Role of Syphilitic Woman as Passive Carrier. H. Pariser, Philadelphia.—p. 243.

Removal of Divalent Cations from Solution by Beef Heart Antigens. L. F. Pierce, Los Angeles, and E. L. Breazeale, Tucson, Ariz.—p. 249.

Experimental Cutaneous Reactions of American Blastomycosis in Guinea Pig. L. M. Nelson, Minneapolis.—p. 257.

*Problem of Treatment Resistant Syphilis: Further Studies on Treatment Resistant Strain of Spirocheta Pallida. H. Beerman and Marie Severac, Philadelphia.—p. 269.

Treatment Resistant Syphilis.—Beerman and Severac began in 1932 to investigate the problem of treatment resistant syphilis in rabbits. The resistant strain of Treponema pallidum was isolated from a patient whose primary and secondary lesions remained uninfluenced by a total of 5.4 Gm. of various arsenicals but whose infection was later satisfactorily controlled by the prolonged use of bismuth salts intramuscularly and intramuscular injections of boiled milk. At first, takes in rabbits with this strain were difficult to obtain; but this decreased as the number of transfers increased, and from the sixteenth to the fifty-seventh animal passage practically every inoculated rabbit became infected. The incubation period, which was variable at first, finally averaged about four weeks. The response of this strain to arsphenamine was controlled by using the Nichols-Hough strain of Treponema pallidum in other rabbits and by using a standard lot of the drug, the minimal sterilizing dose of which has been 14 mg. per kilogram of body weight. Thirteen of 51 rabbits treated with 14 to 30 mg. of arsphenamine per kilogram of body weight failed to be "cured." This refractoriness was sporadic; it was more pronounced in the beginning of the study and occurred less frequently as the strain became adapted to the new host.

Journal of Lab. and Clinical Medicine, St. Louis

28:1-126 (Oct.) 1942

*Heart Disease and Liver Function. M. Bernstein, E. B. Le Winn and S. Simkins, Philadelphia.—p. 1.

Simplified Bedside Test for Latent Jaundice. A. Leslie, New York.—p. 6.

Observations on Additional Instances of Supernormal Phase in Human Heart. H. B. Burchell, Rochester, Minn.—p. 7.

Percutaneous Typhoid Prophylaxis. A. Gelperin and D. Kessler, Cincinnati.—p. 11

Acquired Drug Resistance in Hemolytic Streptococcus. M. Cutts and A. V. Troppoli, Providence, R. I.—p. 14.

Clinical Experiences with Modification of Takata Reaction in Blood and Cerebrospinal Fluid. H. Ucko, London, England.—p. 17.

Effect of Ascorbic Acid (Vitamin C) on Sensitivity to Salicylates in a Case of Rheumatic Fever. L. Pelner, Brooklyn.—p. 28.

Effect of Trasentin A, Trasentin and Morphine on Respiration. N. Tobolowsky, D. Slaughter, T. U. Johnson and R. E. Van Duzen, Dallas, Texas.—p. 31.

Further Studies on Glucophylline. A. H. Maloney, Washington, D. C.—p. 38.

Carcinoma of Stomach Developing in Pernicious Anemia. L. H. Bronstein, New York.—p. 44.

*Guanidine and Its Relationship to Muscular Dystrophy. R. P. MacFate, Chicago.—p. 50.

Comparative Study of Dextrose and Dextrin Tolerance in Patients with Chronic Ulcerative Colitis. R. C. Page, Z. Bercovitz and E. J. de Beer, New York.—p. 66.

Hyperbilirubinemia Following Administration of Sulfonamides. A. Cantarow and C. W. Wirts, Philadelphia.—p. 71.

Heart Disease and Hepatic Function.—The relationship of hepatic function to heart disease, as revealed by the bromsulphalein retention test and by the measurement of the velocity of the blood flow and the venous pressure, was determined by Bernstein and his associates in 29 men and 30 women aged from 19 to 79 years. Fifteen sets of determinations were performed on 15 noncardiac patients; in 14 the bromsulphalein hepatic function test was normal, while 1 had an abnormal bromsulphalein retention without a demonstrable cause. Twelve of thirteen demonstrations in 10 patients with fully compensated heart disease showed agreement and one disagreement between the cardiac status and the hepatic function. In eleven of fourteen determinations on 10 patients with mild cardiac decompensation there was agreement and in three disagreement. Of

fourteen determinations made on 14 patients, six showed the cardiac status and the hepatic function tests to be in agreement and eight showed disagreement. In 13 patients with decided cardiac decompensation eleven of fourteen determinations showed agreement between the cardiac status and hepatic function and three showed disagreement. The results indicate that the bromsulphalein excretion is normal in the absence of heart failure, in mild degrees of cardiac failure the impairment in bromsulphalein excretion is in close parallelism with the status of the circulation, in definite pulmonary congestion the correlation of hepatic function with the circulation is frequently paradoxical and in severe cardiac failure bromsulphalein excretion is usually impaired. Although there was a tendency to parallelism between the bromsulphalein excretion and the degree of cardiac failure, the authors could not determine any mathematical correlation between the two factors.

Guanidine and Muscular Dystrophy.—MacFate studied the effects in guinea pigs of simple guanidine salts on creatine metabolism. The daily administration for several weeks of one third to four fifths of a minimal lethal dose of a toxic guanidine salt produced metabolic and muscular structural changes similar to those found in nutritional muscular dystrophy and in progressive muscular dystrophy. A loss of creatine and phosphate from the muscle and severe disturbances in carbohydrate metabolism and the electrolyte balance occurred. It is suggested that guanidine may lower the permeability of the muscle cell, producing these changes. However, 1 mg. of aminoacetic acid per gram of body weight, administered daily, appeared to afford some protection against the small daily doses of the toxic guanidine salt. Aminoacetic acid seems to delay the progress of a nutritional muscular dystrophy. The abnormal metabolism of guanidine compounds may be an etiologic factor in the production of a progressive muscular dystrophy.

Journal-Lancet, Minneapolis

62:355-388 (Oct.) 1942

Comparative Therapeutic Value and Toxicity of Various Types of Vitamin D. C. Reynolds, New Orleans.—p. 372.
Tuberculosis Control: Introduction. J. A. Myers, Minneapolis.—p. 376.
Id.: Present Status of Tuberculin Test. E. R. Long, Philadelphia.—p. 376.
Id.: Testing for Tuberculosis in Kentucky. L. E. Smith, Louisville, Ky.—p. 379.
Id.: Significance of Tuberculin Test. L. L. Collins, Ottawa, Ill.—p. 380.
Id.: Education About Tuberculosis in 'Teen Age Group: Educational Project in Kanawha County Schools. L. H. Mynes, Charleston, W. Va.—p. 381.
Id.: Summary of Ten Year Mantoux Program in Rural Minnesota. L. S. Jordan, Granite Falls, Minn.—p. 384.

Journal of Pediatrics, St. Louis

21:435-568 (Oct.) 1942

Diagnosis and Management of Severe Infections in Infants and Children: Review of Experiences Since Introduction of Sulfonamide Therapy: I. Sepsis of Lateral Sinus Phlebitis. A. F. Hartmann, Dorothy Wolff and Frances Love, St. Louis.—p. 435.
Vitamin A Absorption and Its Relation to Intestinal Motility in Fibrocystic Disease of Pancreas. L. J. Flax, Marian Barnes and J. L. Reichert, Chicago.—p. 475.
Obesity in Children. I. P. Bronstein, L. J. Halpern and A. W. Brown, Chicago.—p. 485.
*Enterobiasis in Children: Incidence, Symptomatology and Diagnosis, with Simplified Scotch Cellulose Tape Technic. A. H. Jacobs, San Francisco.—p. 497.
Bone Development in Preschool Children. C. L. Wilbar Jr., Honolulu, T. H.—p. 504.
Tetany in Newborn Infant. E. L. Kendig Jr., Richmond, Va.—p. 510.
Weltmann Reaction in Respiratory Diseases in Children. Susan C. Dees, Durham, N. C., and H. Morton, Sarasota, Fla.—p. 514.
Possible Hazards of Repeated Fluoroscopies in Infants. F. Buschke and H. M. Parker, Seattle.—p. 524.

Enterobiasis in Children.—To save time in preparing the NIH swabs and cleaning the used glass rods and also to supply an adhesive surface to which Enterobius vermicularis is more likely to adhere, Jacobs decided to use Scotch cellulose tape. The only materials needed for the technic are a roll of tape, wooden tongue blades and glass microscopic slides. A piece of the tape about the length of the slide is folded over one end of a tongue blade with the nonadhesive surface of the tape against the tongue blade. The ends of the tape can be held in place by the examiner's finger. This is used as an applicator and applied to the perianal folds; the pinworm eggs are picked up by the sticky surface of the tape, which is then removed from the tongue blade and spread out, adhesive surface down, on the slide and examined directly under the low power of the microscope without the use of a coverslip. The slides can be placed in a slide box and examined at one's convenience; they may be kept for many days without any change in the appearance of the ova. In positive cases at least one of the eggs should be examined under high power. The technic was used for the diagnosis of possible enterobiasis in 228 unselected clinic children, and pinworm eggs were found in 31.3 per cent. Of the infected patients, 41.3 per cent had repeated abdominal pains, 49.4 per cent were "nervous," 41.4 per cent were underweight, 38.6 per cent were poor sleepers, 38.6 per cent had anorexia, 21.3 per cent had pruritus ani and 17.3 per cent had enuresis. Of the 40 infected girls, 27.5 per cent had a vaginal discharge. During the study, 14 girls were seen in the clinic with vaginal discharge and 11 of them had oxyuris ova in both perianal and vulvar regions.

Journal of Thoracic Surgery, St. Louis

12:1-108 (Oct.) 1942

*Further Experiences in Surgical Treatment of Subacute Streptococcus Viridans Endarteritis Superimposed on Patent Ductus Arteriosus. A. S. W. Touroff, New York.—p. 1.
Surgical Anatomy of Pulmonary Lobes. E. M. Kent and B. Blades, St. Louis.—p. 18.
Cardiac Arrhythmias and Other Electrocardiographic Changes During Experimental Pneumonectomy. H. L. Cabitt, M. D. Altschule and N. Zamcheck, Boston.—p. 31.
Bronchography: Use of Modified Intranasal Method and Movable Table. B. A. Dormer, J. Friedlander and M. Gibson, Durban, Union of South Africa.—p. 35.
Aspiration of Lower Air Passages Following Endotracheal Anesthesia. C. E. Bird, Providence, R. I.—p. 44.
*Experimental Pulmonary Edema Following Lobectomy and Blood Transfusion. J. H. Gibbon Jr., Mary H. Gibbon and C. W. Kraul, Philadelphia.—p. 60.
"Sniff Test" in Thoracic Surgery: Review of One Hundred and Nineteen Phrenic Nerve Interruptions. J. Greenfield, Cleveland, and G. M. Curtis, Columbus.—p. 78.
Flap Drainage of Residual Tuberculous Cavities. W. L. Rogers, S. J. Shipman and A. C. Daniels, San Francisco.—p. 88.
Acute Putrid Abscess of Lung: V. Hyperacute Variety. H. Neuhof and A. S. W. Touroff, New York.—p. 98.

Streptococcus Viridans Endarteritis.—During the present year Touroff has operated (ductal ligation or division) on 4 additional patients suffering from a relatively early Streptococcus viridans endarteritis superimposed on patent ductus arteriosus. Chemotherapy was given each patient prior to operation. It did not sterilize the blood stream. The operation was ductal ligation in 3 and ductal division in 1. Following operation 3 patients received no chemotherapy and 1 received 10 Gm. of sulfapyridine (on the twelfth postoperative day) because of continuing fever of obscure etiology. However, six postoperative blood cultures had already been reported negative before the drug was given. The 4 patients have recovered and have remained free from infection since operation. Among the author's 8 patients (4 in a previous series) 5 were cured, 2 died from accidental hemorrhage and the fact that 1 patient was not cured is ascribable to the presence of vegetation on the aortic valve at the time of operation. Thus among the 6 who survived 5 were cured. Ductal ligation or division is most likely to be attended with a low morbidity and mortality and a high incidence of cure if it is performed during the early stages of the infection. Since this article was prepared for publication the author has operated on 2 more patients, who recovered.

Experimental Pulmonary Edema.—Recently the Gibbons and Kraul observed 2 patients who died within twelve hours of a bilateral lobectomy. Necropsies were performed on both patients, and the only significant finding was edema of the remaining lobes. To determine whether the fluids administered during and after operation were in any way responsible for the pulmonary edema, the authors performed experiments on anesthetized cats. A blood transfusion of 15 cc. per kilogram of body weight was given to 6 normal cats at a constant rate over a period of half an hour. The saturation of the arterial blood with oxygen was normal before and after the transfusion, and at necropsy no pulmonary edema was evinced. In 9 animals after lobectomy a blood transfusion of 15 cc. per kilogram of body weight was given. Most of the animals exhibited varying

degrees of unsaturation of the arterial blood with oxygen, and 4 of them died shortly after the transfusion was completed. The oxygen capacity of the blood was determined in 14 cats; in 11 it was increased after all the lower lobes and the right middle lobe were removed. In 2 of the 3 remaining cats with no increased capacity subsequent blood transfusion failed to produce evidence of anoxemia and in 1 a mild anoxemia appeared some time after transfusion. They conclude that a blood transfusion of a size well tolerated by normal animals may produce pulmonary edema, a decreased saturation of the arterial blood with oxygen and death.

Journal of Urology, Baltimore

48:343-458 (Oct.) 1942

*Clinical Perinephritis and Its Effect on Blood Pressure. W. F. Braasch and W. W. Wood Jr., Rochester, Minn.—p. 343.
Skin Metastasis from Bladder Tumors. R. C. Atkinson, San Francisco. —p. 350.
Cutaneous Ureterostomy in Active Renal Tuberculosis. F. H. Colby, Boston.—p. 357.
Roentgen Therapy of Carcinoma of Urinary Bladder: Analysis of Fifty-Two Patients Treated with 800 Kv. Roentgen Therapy. F. Buschke and S. T. Cantril, Seattle.—p. 368.
Subcapsular Castration of Carcinoma of Prostate. L. W. Riba, Chicago. —p. 384.
Some Causes of Unsatisfactory End Results After Prostatectomy. G. A. Humphreys, New York.—p. 388.
Dermoid Cysts of Testis. M. B. Dockerty and J. T. Priestley, Rochester, Minn.—p. 392.
*Successful Treatment of Granuloma Inguinale, with Special Reference to Use of Podophyllin. G. C. Tomskey, G. W. Vickery and P. L. Getzoff, New Orleans.—p. 401.
Priapism and Sickle Cell Anemia: Report of Three Cases. P. L. Getzoff, New Orleans.—p. 407.
Use of Vitallium Tubes in Urinary Tract of Dog. J. W. Lord Jr. and J. H. Eckel, New York.—p. 412.
Streptococcus Salivarius in Infections of Urinary Tract and Its Susceptibility to Sulfonamides. E. Neter and Mary Louise Short, Buffalo. —p. 422.
*Theory and Application of Serum "Acid" Phosphatase Determination in Metastasizing Prostatic Carcinoma: Early Effects of Castration. T. J. Sullivan, Ethel Benedict Gutman and A. B. Gutman, New York. —p. 426.

Clinical Perinephritis and Blood Pressure.—Braasch and Wood studied the records of 70 cases of perinephric abscess observed at the Mayo Clinic in the past eleven years in order to determine its effect on blood pressure. Analysis revealed that 6 patients could be classed as hypertensive because of a systolic pressure above 145 mm. and a diastolic pressure above 90 mm. This is an incidence of 8.6 per cent. In 2 of the 6, conclusive evidence was present that hypertension had existed prior to the onset of the perirenal disease. In a third patient other factors apparently were operating to influence the arterial blood pressure. Thus only 3 patients remain in whom association between perinephritis and an elevated arterial blood pressure might be present, an incidence of 4.3 per cent, which is less than half of the incidence of hypertension in a random sample of patients less than 50 years of age who register at the Mayo Clinic. In the authors' opinion this is so low that it should be relegated to chance.

Successful Treatment of Inguinal Granuloma.—The various standardized methods of treating inguinal granuloma are evaluated by Tomskey and his co-workers, who present a new mode of therapy. Complete cures were obtained by 102 patients who were treated with the local application of a mixture of 20 per cent resin of podophyllum in olive oil. The mode of action of the medication awaits further investigation, but the authors believe that the drug acts as a dehydrating agent on the infected granulating tissues and that it also exerts a cauterizing effect. Other active venereal infections (syphilis, venereal lymphopathia and chancroid) were found in 55 of the patients. The patients were previously treated by various accepted methods but no cures were obtained with antimony and potassium tartrate or a combination of antimony and potassium tartrate and surgery even after from two months to almost two years of treatment and hospitalization. Patients, irrespective of the type or the extent of their lesions, treated with resin of podophyllum needed considerably less hospitalization and when discharged were completely healed and have remained so. After healing, no induration, fibrosis or keloid formations were present and the skin was often soft and of normal consistency. The patients treated with resin of podophyllum were also given antimony and potassium tartrate. Several patients were cured with resin of podophyllum alone. Not only was the average hospital stay for those patients who received resin of podophyllum about 35 per cent less but also the favorable response was more than twice that of those who were also treated with antimony and potassium tartrate. In treatment, secondary infection should be eliminated by cleansing the lesion with hydrogen peroxide and hot sitz baths twice a day. The 20 per cent resin of podophyllum in olive oil is applied to the lesion after each bath for five to seven days. Local topical analgesics are recommended for any resultant burning or pain, applied about ten minutes before the resin of podophyllum. When the exuberant granulations have disappeared and a healthy base is evident, resin of podophyllum is discontinued and scarlet red ointment is applied following each bath to stimulate epithelization. The application of resin of podophyllum to any small resistant areas should be continued if a complete cure is to be obtained.

Theory and Application of Serum "Acid" Phosphatase.—Sullivan and the Gutmans give additional data on the use of the serum "acid" phosphatase activity as an aid in the diagnosis of metastasizing prostatic carcinoma. They base their remarks on the results obtained on 200 patients with prostate carcinoma, on 33 of whom castration was performed. The method failed, i. e., values less than 3 units per hundred cubic centimeters were obtained in approximately 15 per cent of 130 patients with definite or suggestive roentgen evidence of metastasis; the remaining 85 per cent had increases in serum "acid" phosphatase, which in extreme cases exceeded 1,000 units per hundred cubic centimeters. Approximately in 89 per cent of 70 patients without roentgen evidence of skeletal metastasis the values were less than 3 units per hundred cubic centimeters. Of a control group of 570 patients with nonprostatic disease, 90 per cent had serum "acid" phosphatase levels of less than 3 units, 7.5 per cent between 3 and 4.9 units and 2.5 per cent more than 5 units. The conclusion drawn is that the method is consistent and specific enough to be a valuable though not an infallible supplement to clinical, roentgen and other studies for the diagnosis of metastasizing prostate carcinoma. The determination has proved useful in corroborating the diagnosis of metastasizing prostatic carcinoma when suggested by other methods, providing evidence of metastasis from prostatic carcinoma before it is demonstrable roentgenographically or by other methods, determining the prostatic or nonprostatic origin of tumors in patients known to have metastasis, differentiating Paget's disease from metastatic prostatic carcinoma, aiding in the selection of patients for prostatectomy, detecting recurrence in prostatectomized patients, aiding in the selection of cases for androgen control and evaluating and regulating androgen treatment. Case reports from the authors' records are cited to illustrate these applications. The important work of Huggins and his associates concerning the effects of castration is confirmed and amplified. Most of the patients showed pronounced clinical improvement following castration.

Kansas Medical Society Journal, Topeka

43:405-440 (Oct.) 1942

Intrathoracic Goiter. C. W. Mayo, Rochester, Minn.—p. 405.
Interrelationships Between Medicine and Psychiatry: Fundamentals of Psychiatry I. W. C. Menninger, Topeka.—p. 407.
Medical Defense in Kansas. F. C. Beelman, Topeka.—p. 412.
Kenny Treatment: Note on Its Use in Kansas Twenty Years Ago. K. A. Menninger, Topeka.—p. 414.
Intravenous Fluids. J. L. Lattimore, Topeka.—p. 416.

Kentucky Medical Journal, Bowling Green

40:393-426 (Oct.) 1942

Organic Factors in Etiology of Mental Disorders. A. Wikler, Lexington. —p. 399.
Report of Case of Rabies. I. J. Hoover, Owensboro.—p. 404.
Diagnosis and Treatment of Epidemiologically Significant Syphilis. C. G. Baker, Lexington.—p. 405.
Industrial Medicine: Physical Examinations of Workers. E. H. Kremer, Louisville.—p. 414.
Id.: Traumatic Wounds; Primary Care. W. Helmus, Louisville.—p. 415.
Id.: Compensable Injuries, Control and Evaluation of Disability. C. L. Nichols, Louisville.—p. 419.
Syphilis Stimulating Disease of Stomach. P. L. Dent, Louisville. —p. 421.
Epilepsy and Dementia Precox and a Few of Its Allegory. J. E. Pinguely, Melbourne.—p. 422.

Medical Annals of District of Columbia, Washington

11:375-418 (Oct.) 1942

Use of Succinylsulfathiazole in Treatment of Amebiasis: Preliminary Report. F. L. Knotts and J. L. Thompson Jr., Fort Belvoir, Va. —p. 375.
Surgical Treatment of Lymphogranuloma Inguinale (Lymphopathia Venereum) of Rectum. R. J. Coffey and L. J. Goffredi, Washington. —p. 378.
*Thorotrast Hepatosplenography as Diagnostic Aid in Solitary Liver Abscess: Report of Four Cases. R. H. Meredith, L. F. Cooper and W. M. Yater, Washington.—p. 382.
Use of Blood Plasma in Surgery. C. S. White and J. J. Weinstein, Washington.—p. 388.
Sickle Cell Anemia and Cholelithiasis: Report of Case. B. F. Schaefer, Washington.—p. 392.

Diagnosis of Liver Abscess.—In the 4 cases discussed, Meredith and his associates made the diagnosis of solitary hepatic abscess by hepatosplenography with thorium dioxide solution as a contrast medium. The precise location of the lesion served as a guide for aspiration. The method appears warranted in all cases in which the diagnosis of hepatic abscess is suspected. The possible potential danger, reported by animal experimenters, from the radioactivity of the thorium that remains in the body indefinitely has not been supported by clinical experience. The microscopic study of tissue from 65 patients injected by Yater and Whitmore with thorium dioxide solution for hepatospenography revealed no evidence of injury to the tissue or any cellular reaction ascribable to the thorium dioxide present. Furthermore, a comprehensive survey of 286 cases covering ten years of experience with the medium in hepatosplenography has revealed no evidence of immediate or remote ill effects in the patients of Yater and Coe. The remarkable point concerning this series of patients was the fact that they have lived longer than was anticipated and have been in moderately good health.

Michigan State Medical Society Journal, Lansing

41:813-892 (Oct.) 1942

Infections of Pharyngomaxillary Space. H. Brunner, Chicago.—p. 841.
Shoveler's Fracture ("Schipperkrankheit"). C. H. Snyder, Grand Rapids. —p. 847.
Needs and Possibilities of Research in Mental Disease. L. Kolb, Washington, D. C.—p. 849.
Embolectomy of External Iliac Artery: Case Report. W. H. Marshall and E. P. Vary, Flint.—p. 856.
Treatment of Typhoid Fever with Typhoid Vaccine: Skin Reaction Controlled Low Dosage Method; Preliminary Report. K. E. Townsend, Detroit.—p. 859.
Mistakes Made in Diagnosis and Estimation of Deafness. D. E. S. Wishart, Toronto, Ont., Canada.—p. 861.
Some Obstetric Opinions. J. R. McCord, Atlanta, Ga.—p. 866.
Treatment of Parkinson's Disease: Comparison of Atropine Sulfate and Wines of American and Bulgarian Belladonna. S. S. Bohn, Detroit.—p. 871.

Military Surgeon, Washington, D. C.

91:379-498 (Oct.) 1942

The Medical Soldier and the Infantryman. E. E. Hume.—p. 379.
Outbreak of Jaundice in the Army: Supplement to Circular Letter No. 45.—p. 386.
Malignant Tumors of Skin. L. H. Warren.—p. 393.
Drivers' Aptitude Tests of Third Armored Division. W. G. Reid. —p. 401.
Coronary Heart Disease. H. P. Marvin.—p. 411.
Salvaging the Nation's Man Power. Helen S. Willard.—p. 416.
Acrylic Jacket Crown: Practical Technic. F. W. Stevens.—p. 418.
Deep Infections of Neck. M. B. Stewart.—p. 426.
Contact Reporting in Venereal Disease Control: Function of the Medical Officer. F. W. Reynolds.—p. 432.
Cases Rejected for Army Service on Basis of Chest Films Alone. A. R. Koontz.—p. 440.
Preliminary Study Using Short Objective Measure for Determining Mental Deficiency in Selective Service Registrants. F. J. Koenig and J. Smith.—p. 442.
Discussion of Chigoe (Tunga Penetrans) Based on Experiences in British Guiana. C. O. Bruce, T. D. Knigin and S. F. Yolles.—p. 446.
Experiences in Military Psychiatry. F. P. Pignataro.—p. 453.
John Mills Browne—Surgeon General, U. S. Navy (1888-1893). L. H. Roddis.—p. 460.

Missouri State Medical Assn. Journal, St. Louis

39:333-358 (Nov.) 1942

Surgical Lesions of Ileum. A. P. Stout, New York.—p. 333.
Faith, Hope and Cure Alls. K. W. Brimmer, Washington, D. C.—p. 335.
Infantile Paralysis in Missouri. A. O'Reilly, St. Louis.—p. 338.
Modern Concepts in Treatment of Burns. R. O. Pearman and F. G. Thompson Jr., St. Joseph.—p. 342.

New Jersey Medical Society Journal, Trenton

39:517-566 (Oct.) 1942

*Neuroses and Psychoses in Wartime. C. M. Trippe, Asbury Park. —p. 524.
Nocturnal Angina: Symptom of Coronary Insufficiency. B. Rubin, South River.—p. 529.
Indications for Splenectomy in Gaucher Splenomegaly. A. O. Wilensky, New York.—p. 531.
New Use for Wangensteen Suction Drainage. C. R. Weinberg and I. L. Sperling, Newark.—p. 538.

Neuroses and Psychoses in Wartime.—Trippe states that the chief predisposing causes of neurosis and psychosis in wartime as in peacetime are neuropathic or psychopathic inheritance and a previous nervous or mental breakdown. Had the 1917-1918 induction board examiners used present day methods, three billion dollars would have been saved the United States for the care and compensation of 97,000 preventable mental casualties. Now, rejected neuropsychiatric selectees are returned to their communities to share with others who are easily emotionally dislocated benefits not afforded at the battle front. The preventive measures to be constantly employed among all civilians are play, work and knowledge. Recreation should not be merely a side issue. It should be constructively planned to suit each individual. Work should be of the type in which people feel they are doing something for the cause in their all out effort directed toward future peace. Knowledge is an antidote against poisoned morale, and too much can never be attained, especially for confidence in the body politic against the wide extent of subtle enemy propaganda. The Association for the Advancement of Psychoanalysis best sums up the attitude America must recognize: Under war conditions an increase in anxiety and tension is natural and inevitable. Unless this is realized, an individual might consider himself cowardly and contemptible when he is actually sharing a common experience. If anxiety incapacitates an individual, then it is most probably not associated with the war and represents a personal problem. Foolhardiness and impulsiveness are not cures for fear. Inactivity and isolation from the group beget anxiety.

New York State Journal of Medicine, New York

42:1887-1982 (Oct. 15) 1942

Epidemiology of Diarrheas in New York City. S. Frant, New York. —p. 1911.
Diarrhea from Point of View of a Physician. S. Kimball, Buffalo. —p. 1915.
Significance and Interpretation of Diarrheas Encountered in Proctologic Practice. M. S. Kleckner, Allentown, Pa.—p. 1919.
Roentgen Ray: Aid in Study of Diarrhea. J. M. Flynn, Rochester. —p. 1926.
Pathogenesis of Fetal Erythroblastosis. P. Levine, Newark, N. J. —p. 1928.
Movements of Body Water in Relation to Anesthesia. H. G. Barbour, New Haven, Conn.—p. 1936.
Addison's Disease in the Negro: Report of Three Cases and Review of Literature. J. R. Lisa, C. Solomon, New York, and E. J. Gordon, Washington, D. C.—p. 1940.
Modern Aspects of the Hearing Aid Problem. T. H. Halsted and F. M. Grossman, New York.—p. 1944.
Sedimentation Rate in Gastrointestinal Disease. W. F. Lipp and A. H. Aaron, Buffalo.—p. 1951.
Congenital Tuberculosis. G. L. Robillard and S. Z. Imprescia, Brooklyn. —p. 1955.

North Carolina Medical Journal, Winston-Salem

3:539-578 (Oct.) 1942

General Surgery and Surgical Specialties. H. A. Royster, Raleigh. —p. 539.
Brief Discussion of Bronchiectasis. M. D. Bonner, Jamestown.—p. 543.
Bleeding Associated with Intrauterine Death of Fetus. F. R. Lock, Winston-Salem.—p. 547.
Threatened Abortion. R. B. Dunn, Greensboro.—p. 549.
Immediate Postoperative Feeding in Abdominal Surgery. A. Webb Jr., Raleigh.—p. 551.
Hookworm: Etiologic Factor in Duodenitis. C. F. Strosnider, Goldsboro.—p. 554.
Harmful Effect of Tobacco on Course of Buerger's Disease: Report of Case with Recurrence in Man of Unusual Height and Weight. R. H. Owen, Canton.—p. 555.
Recovery from Streptococcus Viridans Bacteremia After Sulfanilamide: Report of Case. W. M. Johnson, Winston-Salem.—p. 558.
Economy in Vitamin Medication. J. B. Stevens, Greensboro.—p. 560.
Hypnosis. L. Alexander, Durham.—p. 562.

Ohio State Medical Journal, Columbus

38:989-1084 (Nov.) 1942

Deficiency Diseases: Incidence at Cincinnati General Hospital. M. A. Blankenhorn, Cincinnati.—p. 1005.

Chemistry of Pollen Extracts: I. Studies with Activated Charcoal and Ragweed Pollen Extract. E. A. Brown and N. Benotti, Boston. —p. 1011.

Gallbladder Disease and Pregnancy. L. H. Biskind and H. H. Pevaroff, Cleveland.—p. 1013.

Management of Drug Eruptions. A. R. Cukerbaum, Youngstown. —p. 1016.

Preparation of Patient for Anesthesia. J. H. Bennett, Cincinnati. —p. 1019.

Cancer of Vulva. J. J. McDonough, Youngstown.—p. 1022.

Importance of Purposeful Splinting Following Injuries of Hand. C. D. Hoy, Columbus.—p. 1025.

Boron as Trace Element. J. Forman, Columbus.—p. 1026.

Psychology of the Sick. C. W. Sawyer, Marion.—p. 1028.

Examining for Life Insurance. J. Dittrick, Cleveland.—p. 1033.

Pulmonary Actinomycosis: Case Record Presenting Clinical Problems. F. T. Kapp, Cleveland.—p. 1036.

Oklahoma State Medical Assn. Jour., Oklahoma City

35:411-452 (Oct.) 1942

Isolation as Aid in Treating the Mental Patient. C. E. Leonard, Oklahoma City.—p. 411.

Clinical Diagnosis of Ulcer of Meckel's Diverticulum. J. G. Matt, Tulsa.—p. 414.

Phrenic Nerve. F. P. Baker, Talihina.—p. 417.

Fluoroscopic Survey of Postnatal Syphilis in Health Department Clinic. D. V. Hudson and S. C. Venable, Tulsa.—p. 419.

Pennsylvania Medical Journal, Harrisburg

46:1-80 (Oct.) 1942

*Use of Sulfonamides in Local Treatment of Burns. J. E. Rhoads, W. A. Wolff and W. E. Lee, Philadelphia.—p. 13.

Pathology Among Institutionalized Psychotics. T. K. Rathmell and M. M. Lieber, Sharon.—p. 17.

Waters' Extraperitoneal Cesarean Section: Report of Three Cases. C. C. Briscoe, Philadelphia.—p. 19.

Delayed Wound Healing Associated with Scurvy: Case Reports. E. L. Housel and L. H. Clerf, Philadelphia.—p. 21.

Sulfonamides and Local Treatment of Burns.—According to Rhoads and his associates, the use of sulfonamide compounds in the local treatment of burns has not, in their hands, obviated the necessity for skin grafting, but they believe that their use has reduced the amount of skin grafting necessary and that their value in preparing granulating surfaces for grafting and in effecting bacteriostasis while the grafts are taking has been immeasurable. They have employed sulfanilamide, sulfathiazole and sulfadiazine in powdered form as a primary and as a secondary dressing after other forms of treatment. The results have been superior to those that they obtained by other methods. Spontaneous epithelization without grafting took place more often and pinch grafts tolerated the sulfanilamide well. The drug has been helpful in depressing the infecting organisms during the five days between the application of the graft and the first dressing; thus successful grafting at an earlier stage was possible. The drugs are freely absorbed through large burns and may give rise to drug fever and other toxic effects. Therefore, in view of the hepatic injury in extensive burns and the occasional toxic hepatitis following some of the sulfonamides, the use of the drugs primarily in extensive burns should be approached cautiously. When an occlusive dressing and the sulfonamide effect is desired, sulfadiazine in triethanolamine, as introduced by Pickrell, should be considered.

Public Health Reports, Washington, D. C.

57:1479-1518 (Oct. 2) 1942

Incidence of Pneumonia as Recorded in National Health Survey. R. H. Britten.—p. 1479.

Infant Mortality in Rural and Urban Areas. H. J. Sommers.—p. 1494.

Ornithodoros Parkeri and Relapsing Fever Spirochetes in Southern Idaho. G. E. Davis.—p. 1501.

57:1519-1558 (Oct. 9) 1942

Cultural Characteristics of Zooglea-Forming Bacteria Isolated from Activated Sludge and Trickling Filters. Elsie Wattie.—p. 1519.

Chemotherapeutic Action of a N-Phosphoryl Derivative of 4-4'-Diaminodiphenylsulfone. M. I. Smith, S. M. Rosenthal and E. L. Jackson, —p. 1534.

Surgery, Gynecology and Obstetrics, Chicago

75:547-674 (Nov.) 1942

*Analysis of Relationship of Surgery and Gastroscopy in Ninety-Five Cases of Gastric Tumor. R. Schindler and P. Letendre, Chicago. —p. 547.

*Post-Traumatic Dystrophy of Extremities: Sudeck's Atrophy. D. S. Miller and G. de Takats, Chicago.—p. 558.

Improved Method of Measuring Potential Difference Across Human Gastric Membranes and Its Clinical Significance: Preliminary Report. E. N. Goodman, New York.—p. 583.

Clothespin or Inclusion Graft for Spondylolisthesis or Laminal Defects of Lumbar Spine. D. M. Bosworth, New York.—p. 593.

Relationship Between Clinical and Roentgenologic Findings in Bone Metastases. J. Borak, New York.—p. 599.

Prolapse of Efferent (Distal) Segment of Bowel After Colostomy. J. L. Keeley, Chicago.—p. 605.

*Experimental Crushing Injury: Peripheral Circulatory Collapse and Other Effects of Muscle Necrosis in Rabbit. E. G. L. Bywaters and G. Popjak, London, England.—p. 612.

Routine Abdominal Panhysterectomy as Prophylaxis Against Cancer of Cervical Stump. K. H. Martzloff, Portland, Ore.—p. 628.

Repair of Incontinent Sphincter Ani. P. C. Blaisdell, Pasadena, Calif. —p. 634.

Complications of Inferoanterior (Axillary) Dislocation of Shoulder Joint as Demonstrated by Roentgenograms. M. D. Sachs and H. A. Hill, San Francisco.—p. 639.

Beaded Wires in Closed Reduction of Fractures of Leg. C. N. Pease, Chicago.—p. 647.

Combined Spinal and Intravenous Anesthesia for Operations on Colon. B. M. Anderson, L. H. Mousel and C. W. Mayo, Rochester, Minn. —p. 651.

Intravenous Amino Acid Administration in Surgical Patients Using Enzymatic Casein Digest. C. E. Gardner Jr. and J. C. Trent, Durham, N. C.—p. 657.

Surgical Gloves and Wound Infections. L. A. Weed and Jessie L. Groves, Indianapolis.—p. 661.

Unreliability of Blood Findings as Criteria of Burn Shock in Rabbits. M. D. Bosse, P. Gross and M. L. Hagan, Pittsburgh.—p. 665.

Surgery and Gastroscopy in Gastric Tumor.—Schindler and Letendre compare the gastroscopic with the surgical observations in 95 cases of gastric tumor, 91 of which were cancerous. In 5 of the 91 cases of gastric cancer the lesion was not seen gastroscopically and in 5 others the lesion seen was wrongly interpreted. Of the others, a sarcoma was mistaken for a polyposis, 1 benign submucosal tumor and 1 benign mucosal tumor were diagnosed correctly and 1 benign mucosal tumor was called cancer at gastroscopy. The number of gastroscopic errors can be reduced with increasing experience. In 4 of the 95 cases the gastroscopist did not commit himself as to the nature of the lesion. In 3 cases gastroscopy revealed lesions not palpated or seen by the surgeon at laparotomy. Further examination proved the lesions to be present. Roentgenography and gastroscopy will yield best results in the diagnosis of gastric tumors when used together. In the series of 91 carcinomas, fifteen failures at the first roentgen examination are compared with ten failures at the first gastroscopic examination. The size and the site of the tumor were determined satisfactorily by gastroscopy. The gross type of carcinoma should be diagnosed at gastroscopy only if the whole circumference of the tumor can be seen.

Post-Traumatic Dystrophy of Extremities.—Miller and de Takats discuss the signs and alterations that may contribute to a better understanding and earlier treatment of Sudeck's atrophy. In its milder forms the syndrome is far from being rare. When a sprain or a blunt or minor injury does not show a normal course of events but is characterized by excessive pain, vasomotor phenomena and increased pulsations of peripheral vessels, an early reflex dystrophy should be suspected. The differentiation of an early Sudeck's atrophy from traumatic hysteria is often difficult, as the emotional status of many of these patients is often unstable. The "nervousness" and "excitability" in the late cases may just as well be the result of many months of suffering and not the cause of the syndrome, which most neurologists still maintain. The osteoporosis is not typical for the syndrome. It does not appear early. When it appears in its spotty form in the small bones of the hand and foot or in the lower metaphysis of the bones of the lower arm and leg, four to six weeks after the injury, it is rather characteristic. A diagnosis then can be made but only in conjunction with the clinical phenomena. In the later stages, when the bone atrophy

is diffuse, a roentgen differentiation from other forms of atrophy hardly seems possible. Minor, partial injuries of peripheral nerves coursing superficially between the skin and the bone may sometimes be the initial stimulus for the vasomotor phenomena. The diagnosis of such partial nerve injury would be made more often in the dorsal interosseous nerve in Colles' fracture, the superficial radial and ulnar branches in twists and torsions of the wrist and in injuries to the superficial peroneal, posterior tibial and saphenous nerves (which are often stretched, contused or surrounded by a perineural hematoma) if the examination should be directed toward them in cases of severe pain following trauma. The best prevention for Sudeck's atrophy seems the early and complete fixation of all injuries, without interfering with motion and permitting weight bearing, as Boehler recommended, and infiltration of the site of injury with procaine hydrochloride. Whatever the explanation for vasomotor disturbance in Sudeck's atrophy (arteriolar dilatation coexisting with a capillary spasm), repeated sympathetic block in the earlier stages and sympathectomy in the later, more intractable, cases have been of decided benefit. The infiltrations can be followed by mild physical therapy, which, if used alone, often aggravates the pain and muscular spasm. When organic changes are present, such as shortening of tendons, shrinking of joint capsule, ankylosis and faulty position, orthopedic care is required for full functional recovery after sympathectomy.

Experimental Crushing Injury.—Bywaters and Popjak describe a method of producing graded injury in the rabbit. It consists in winding a rubber band round the leg so as to produce an ischemia, which is maintained for four and five hours. The resulting course is hemoconcentration and loss of plasma into the injured area, which becomes swollen and doughy. Azotemia, which is thought to be due in part to the depressed circulation but mostly to the increased tissue breakdown, occurs. Other manifestations of the latter are creatinuria and a depression of the carbon dioxide combining power of the plasma, associated with an increased urinary acidity. There is no obviously gross impairment of renal function that could be measured by the power to concentrate urea, although a few hyaline and granular casts, sometimes accompanied by a trace of proteinuria, appear. The condition differs from the human condition of "crush syndrome" only in that renal failure and myohemoglobinuria are absent, and as there is ample anatomic reason in the rabbit for myohemoglobinuria to be absent it seems possible that these two negative "occurrences" may be causally related to each other.

Surgery, St. Louis

12:523-684 (Oct.) 1942

Internal Wiring Fixation of Facial Fractures. W. M. Adams, Memphis, Tenn.—p. 523.

*Bronchial Factor in Pulmonary Embolism. J. H. Jesser and G. de Takats, Chicago.—p. 541.

Regional Lymphatic Metastasis of Carcinoma of Gastrointestinal Tract. E. B. Kay, Ann Arbor, Mich.—p. 553.

Double Tube Method for Drainage and Feeding Following Gastric Resection or Gastroenterostomy. W. L. Mersheimer, New York. —p. 563.

Potential Closed Duodenal Loop in Gastric Resection. D. Lynn, Detroit; L. J. Hay and O. H. Wangensteen, Minneapolis.—p. 566.

Treatment of Acute Appendicitis in Children as Influenced by Chemotherapy. C. A. Wattenberg and P. Heinbecker, St. Louis.—p. 576.

Unusual Anomaly of Bile Ducts in Adult with Obstructive Jaundice: Report of Case. O. W. Niemeier, Hamilton, Ont., Canada.—p. 584.

Treatment of Common Duct Stone Missed at Operation. H. B. Morton, Lincoln, Neb.—p. 591.

Effect of Anesthetics on Gastric Tonus and Motility, with Special Reference to Acute Gastric Dilatation. C. R. Johnson and F. C. Mann, Rochester, Minn.—p. 599.

*Traumatic Rupture of Pregnant Uterus Resulting from Automobile Accident. R. B. Woodhull, Minot, N. D.—p. 615.

Epispadias with Incontinence in Male. J. E. Dees, Durham, N. C. —p. 621.

New Skin Varnish for Maintaining Sterility of Operative Field. A. D. Ecker, Syracuse, N. Y.—p. 631.

*Consideration of Therapy in Staphylococcic Infections. R. H. Rigdon, Memphis, Tenn., and P. F. Stookey, Kansas City, Mo.—p. 635.

Bronchial Factor in Pulmonary Embolism.—Jesser and de Takats observed the behavior of the bronchial tree when pulmonary embolism is produced in dogs weighing from 10 to 15 Kg. The embolus was produced by injecting 0.5 cc. of a mixture of equal parts of barium sulfate, iron perchloride and isotonic solution of sodium chloride into the femoral vein. A powerful bronchoconstriction was produced during embolism. This could be abolished by bilateral vagal section and often by sufficient doses of atropine. Mechanical obstruction to the trachea did not produce bronchial spasm. Papaverine usually failed to protect the bronchial tree from this reflex spasm. Clinically the suppression of the widespread autonomic reflexes which occur within the distribution of vagal fibers would decrease the morbidity and mortality from pulmonary embolism; at least atropine did in the animal experiments. Its clinical use, in the presence of bronchial obstruction and hypersecretion, may be objected to by those who feel that the drug increases the viscosity of the bronchial mucus and hinders evacuation. The 28 patients with pulmonary embolism observed at St. Luke's Hospital received the atropine-papaverine mixture. It was given immediately after the embolus was recognized and for four to five days thereafter, three times a day. No massive or patchy atelectasis was seen in this group of patients, indicating that at least this medication does not increase bronchial obstruction to a harmful degree.

Rupture of Pregnant Uterus.—Woodhull reports that the uterus of a pregnant woman was ruptured in an automobile accident; the erroneous diagnosis of premature separation of the placenta was made because the patient made a rapid recovery on only supportive treatment. It was assumed that uterine rupture occurred at the time of the accident as the result of a blow on the abdomen. After the fetus and a portion of the placenta were extruded into the abdominal cavity the uterus apparently clamped down very rapidly, causing only a minimal loss of blood. Fetal death must necessarily have taken place within several minutes after the accident. From the standpoint of diagnosis the patient did not exhibit the usual signs associated with rupture of the uterus; that is, evidence of intra-abdominal hemorrhage, shock, accumulation of blood under the diaphragm, abdominal rigidity, pain radiating to the shoulder or vaginal bleeding. The absence of these signs masked the true gravity of her condition and led to the early mistaken diagnosis. It was only after inflammatory reactions and toxic absorption were in evidence that operation was performed. Once a diagnosis of uterine rupture is made, the decision whether to remove the uterus or to attempt repair is influenced by the parity of the patient and her desire for future pregnancies. Although the outcome in his case was satisfactory, the author emphasizes the fact that early diagnosis and prompt operative treatment are of the utmost importance. First and foremost, shock should be controlled by intravenous fluids and blood transfusion, and a laparotomy should be performed as soon as the patient's condition permits. Clamping the uterine arteries through the vagina while preparations for adequate surgery are in progress has been attempted by some men with success.

Therapy in Staphylococcic Infection.—Rigdon and Stookey used staphylococcus antitoxin in the treatment of **2** patients with staphylococcic septicemia. The dose of the antitoxin should always be sufficient to produce an excess of antitoxin in the circulating blood. The minimal dose should be 100,000 units preferably given intravenously. In severe infection with profound toxemia 300,000 to 400,000 units of the antitoxin may be required. One important way in which staphylococci may have an influence on the host is through the effect of their toxin on the parenchymatous tissue. Their exotoxin may be neutralized by specific antitoxin given before the toxin becomes fixed in the tissues. Toxin apparently is present in more than 90 per cent of patients with staphylococcic septicemia. It can produce death or it may be only of secondary importance in the pathologic processes. The effect of chemotherapeutic agents depends on their inhibitory influence on bacterial growth. They do not neutralize staphylococcus toxin. Combined chemotherapy and serotherapy may offer the best results in staphylococcic septicemia. The efficacy of any treatment is in direct ratio to the duration of the infection, the toxin producing ability of the organism and the resistance of the host. The therapeutic response is best when treatment is instituted early. Chemotherapy and serotherapy are only adjuncts to surgery.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

Archives of Disease in Childhood, London

17:111-174 (Sept.) 1942

Clinical and Bacteriologic Survey of Pneumonia in Childhood. Esther Hendry.—p. 11.
Dementia Infantilis with Cortical Dysrhythmia. A. Kennedy and D. Hill. —p. 122.
Hospital Diarrhea. P. Evans.—p. 130.
Micro Method for Estimation of Sedimentation Rate of Red Cells. Hilda Trought.—p. 136.
Some Social Aspects of Infant Feeding. I. Gordon.—p. 139.

Brain, London

65:115-232 (June) 1942

Studies in Human Vestibular Function: I. Observations on Directional Preponderance ("Nystagmusbereitschaft") of Caloric Nystagmus Resulting from Cerebral Lesions. G. Fitzgerald and C. S. Hallpike.—p. 115.
Id.: II. Observations on Directional Preponderance of Caloric Nystagmus ("Nystagmusbereitschaft") Resulting from Unilateral Labyrinthectomy. T. E. Cawthorne, G. Fitzgerald and C. S. Hallpike.—p. 138.
Id.: III. Observations on Clinical Features of "Ménière's" Disease, with Special Reference to Results of Caloric Tests. T. E. Cawthorne, G. Fitzgerald and C. S. Hallpike.—p. 161.
*Chronic Thyrotoxic Myopathy: Report of Three Cases with Review of Previously Reported Cases. D. McEachern and W. D. Ross.—p. 181.
Primary Degeneration of Spinal Cord in Monkeys: Study in Comparative Pathology. A. E. Hamerton.—p. 193.
Aphasia in Children. E. Guttmann.—p. 205.
Cerebello-Olivary Degeneration: Example of Heredofamilial Incidence. F. P. Weber and J. G. Greenfield.—p. 220.

Chronic Thyrotoxic Myopathy.—McEachern and Ross report 3 cases of chronic thyrotoxic myopathy and review the 10 described previously in the literature. This disorder resembles progressive muscular atrophy but is unlike it, as it is amenable to treatment. The chief features of the 13 cases are as follows: The sex was predominantly male (11 to 2). The age of 1 of the patients was 24 and the other 12 were between 39 and 62 years old. The main symptoms were weakness and loss of weight with muscular wasting, sometimes symptoms suggestive of hyperthyroidism. The onset was gradual, usually leading to hospitalization in a year. The pulse rate was elevated, and often the pulse pressure was increased. Tremor of the outstretched hands was prominent and general muscular wasting with fasciculation was pronounced in the shoulder and pelvic girdles and less so peripherally in the small muscles of the hands and feet. The basal metabolic rate was elevated from + 14 to + 68 per cent in 12 and to + 100 in 1. The blood cholesterol was low or normal, and the dextrose tolerance was normal or reduced. Creatinuria was present, and glycosuria in some. Thyroidectomy resulted in complete recovery. The 3 patients who were not submitted to operation died, 2 from respiratory paralysis. The muscular weakness and fatigability may temporarily respond to a prostigmine preparation. Fasciculation appears to be of peripheral origin, suggesting that there is an increased concentration of acetylcholine at the neuromuscular junctions or a generally increased sensibility of muscle fibers to the chemical transmitter due to metabolic causes and not to denervation. The increased basal metabolism cannot be attributed to fasciculation, as cases of amyotrophic lateral sclerosis show no such increase despite equally active and widespread muscular twitching.

British Journal of Ophthalmology, London

26:433-480 (Oct.) 1942

Statistical Analysis of 3,219 Persons Certified Blind at Regional Clinic for Certification of the Blind, Glasgow and Southwest Scotland, During Period 1929-1935: VI. Summary and Conclusions. J. Marshall and H. E. Seiler.—p. 433.
Four Unusual Cases of Conjunctivitis. E. F. King.—p. 467.

British Journal of Tuberculosis, London

36:99-152 (July) 1942

Benign Serous and Purulent Pleural Effusions (Including Tuberculous Empyema): Plea for Conservative Treatment. F. G. Chandler. —p. 103.
Extrafascial Apicolysis with Thoracoplasty: Indications, Technic and Complications. C. P. Thomas and W. P. Cleland.—p. 109.
Treatment of Intestinal Tuberculosis by Pneumoperitoneum. L. Roberts. —p. 138.

British Journal of Urology, London

14:113-152 (Sept.) 1942

Postprostatectomy Obstruction. T. Millin.—p. 113.
Primary Carcinoma of Ureter: Case Report. H. N. Daniel.—p. 124.

British Medical Journal, London

2:357-384 (Sept. 26) 1942

British Tradition and the New Outlook. B. Whitehouse.—p. 357.
Malingering. R. Good.—p. 359.
Foreign Bodies in Alimentary Tract. G. O. Chambers.—p. 362.
Periodic Medical Examination. F. Ellis.—p. 365.

2:385-416 (Oct. 3) 1942

Wartime Arrangements for International Biological Standards and New Standard for Pituitary (Posterior Lobe) Preparations. H. H. Dale. —p. 385.
Nontouch Technic, Special Reference to Operative Treatment of Simple Fractures. H. A. T. Fairbank.—p. 388.
Surgical Amputations and Fitting of Artificial Limbs. A. W. J. Craft. —p. 389.
*Renal Impairment Due to Crushing Limbs in Anesthetized Dogs. M. Grace Eggleton, K. C. Richardson, H. O. Schild and F. R. Winton. —p. 392.
Variations in Respiratory Rhythm of Prognostic Significance in Malignant Hypertension. H. O. Gunewardene.—p. 393.
Vaccination in Glasgow Docks. G. Buchanan and S. Laidlaw.—p. 394.

Renal Impairment Due to Crushing Limbs.—According to Eggleton and her colleagues, impairment of renal function in dogs under soluble pentobarbital anesthesia ensues after four to five hours during which time both hind limbs have been tightly bound with rubber tubing from the ankle to the hip and the thigh muscles have been compressed in a vise and hammered for a few minutes. Removal of the compression is followed by a definite fall in arterial pressure and by anuria or severe oliguria. In the latter event the urine is deeply pigmented, presumably with myohemoglobin, and the creatinine clearance is low, which might be attributed in part to the low arterial pressure. Restoration of the arterial pressure with intravenous gum-saline solution of ox serum usually initiates or increases the urinary flow; but even if the flow is raised to its initial value with diuretics the creatinine clearance, and therefore the concentrating power of the kidney, recovers to only about one fourth of its original value. Microscopically, the kidneys contained a material within the lumens of the tubules which might have been capable of blocking some of the tubules. The material was particularly concentrated in the terminal portion of the proximal convoluted tubules. There was no consistent relation between the extent of the deposit and the impairment of renal function. In the only dog in which high doses of diuretics would not initiate urinary flow there were mitochondrial changes in the proximal tubule cells, indicating the action of a poisoning agent. The available evidence from the study of the dogs appears to show that the renal damage is of the same kind as that in man after comparable prolonged crush injury to the limbs. The evidence suggests that the main factor in the injury may be concerned with an increased permeability of the renal tubules due to a toxic agent released from the damaged limbs.

2:417-444 (Oct. 10) 1942

Tuberculosis in London in Wartime. W. A. Daley and B. Benjamin. —p. 417.
*Wartime Dermatology with Plea for Economy. R. W. Carslaw.—p. 420.
Ligature of Innominate Artery for Right Subclavian Aneurysm: End Result. W. I. de C. Wheeler.—p. 422.
*Cerebrospinal Fever: Review of 500 Cases Treated by Chemotherapy Without Intrathecal Serum. G. E. Harries.—p. 423.
Mangled Forearm: Treatment in Skeleton Splint with Fixed Skeletal Traction. D. Brown.—p. 425.

Wartime Dermatology.—Carslaw discusses his experience with diseases of the skin which began just before the present war. The first part of his experience consisted of six months afloat in a cold or extremely cold climate with a personnel of approximately 500 men, the second part of eighteen months was that of a skin department of a large naval hospital at home and the third consisted of six months afloat in the tropics with a personnel of approximately 1,600 men. Little contact was made with centers of population during either time afloat, and fresh food was intermittently available. During the first period the few cases that were encountered consisted of impetigo and scabies and several cases of dermatitis of the hands, apparently

due to change from civil to service occupation. During the second part 1,149 cases were seen—652 as inpatients and 497 in consultation. There were (in order of frequency) cases of dermatitis from all causes, scabies, impetigo and mycosis. During the last period 349 cases of mycosis, scabies, miliaria rubra or impetigo were encountered. The following points, according to the author, are of practical value in service wartime dermatology: (1) economy of loss of men hours and of drugs is of national importance, (2) the bulk of medical stores must be kept small, (3) simplicity and, when possible, standardization ease the burden of an overtaxed nursing staff and (4) early diagnosis and treatment save loss of man hours. Ointments could, he feels, be largely discarded, particularly in summer and in hot climates, mercury replaced by aniline dyes and the production of starch poultices curtailed. The best results were obtained by the use of a comparatively small number of remedies, and simplicity saved the time of nursing and dispensing staffs. Early diagnosis and treatment mean a smaller area to treat and therefore a saving of supplies and time lost. In many ways life has been made more simple by rationing in domestic life, and a plea is made that the treatment of cutaneous conditions could and should be simplified to conform with the national war effort. For the treatment of mycosis chrysarobin was used, as the cases were unusually severe and numerous.

Cerebrospinal Fever.—From January 1940 through February 1942, 500 patients with cerebrospinal fever were admitted to the Cardiff City Isolation Hospital. They were treated by chemotherapy, Harries says, without antimeningococcus serum intrathecally. The ages of the patients ranged from an infant of 6 weeks who recovered completely to a person of 70 who died. All patients, even those who were moribund and died within a few minutes of admission, were included in the group of 500. The total number of deaths was forty-three. Sulfapyridine was employed in the treatment of 471 and sulfathiazole for the others. Sulfathiazole was as effective in promoting recovery and was less prone to cause nausea and vomiting. The drug was given by mouth in 2 Gm. doses on admission and repeated in four hours' time; then 1 Gm. every four hours for the next seventy-two hours; then 0.5 Gm. was given for a further three days. After the first 250 patients were treated the dose was increased to 2 Gm. every four hours for four doses and then 1 Gm. every four hours for ninety-six hours, followed by 0.5 Gm. every six hours for a further three days. The increased dosage had a slight effect in diminishing recurrences and complications, such as arthritis. Children less than 12 were given half the adult dosage, and infants less than 1 received one fourth of the adult dose. In all, 1,935 lumbar punctures were performed without any untoward effect. No general anesthetic was administered. Apart from relieving headache, the reduced intracranial pressure was considered less damaging to the nervous tissue. The cerebrospinal fluid furnished a satisfactory guide to the progress of the disease. No patient was regarded as out of danger if the sugar had not returned to normal. Only six ventricular and five cisternal punctures were necessary. If the patient was comatose the tablets were crushed and given intranasally. If vomiting occurred after ingestion of the drug or the patient was delirious and nasal feeding was difficult, the sodium salt of sulfapyridine was given by intramuscular injection; but as sloughing often ensued in spite of care, it was discontinued and the sodium salt in equivalent doses was injected intravenously with three times its volume of isotonic solution of sodium chloride. Severely ill or greatly dehydrated patients were given the sodium salt of sulfapyridine intravenously in about 500 to 1,000 cc. or more of isotonic solution of sodium chloride in 5 per cent dextrose solution by the vacoliter drip method. The ingestion of fluid was encouraged. The patients who had such complications as arthritis or iridocyclitis during convalescence were given a second course of chemotherapy. If bromides were given as sedatives the sodium salt rather than the potassium salt was administered. No person in attendance contracted the disease. Morphologic meningococci were found in 465 cases, or 93 per cent. Material for cultures was obtained from 214; 93 per cent belonged to group 1, 3.7 per cent to group 2 and 3.3 per cent were inagglutinable. Clinically, the various strains seemed to be of equal virulence.

Lancet, London

2:355-384 (Sept. 26) 1942

The Thomas Splint in Treatment of Fractured Femur. W. S. Diggle. —p. 355.
Bronchography in Children. C. Elaine Field.—p. 357.
Sulfapyridine Anuria: Fatal Case. J. Carson and G. S. Smith.—p. 359.
Id.: Treated by Cystoscopy and Ureteric Catheterization. R. C. S. Benson and R. C. Percival.—p. 360.
*Water Borne Outbreak of Paratyphoid B Fever. D. J. Jones, P. G. H. Gell and R. Knox.—p. 362.
Portable Apparatus for Continuous Intravenous Therapy. B. G. B. Lucas and A. L. Sims.—p. 364.
Preparation of Antiscorpion Serum: Use of Atropine and Ergotoxine. A. H. Mohammed.—p. 364.
Plasmodium Falciparum Malaria: Case. J. E. Murray and P. G. Shute. —p. 365.

Water Borne Outbreak of Paratyphoid B.—Jones and his colleagues report the occurrence of paratyphoid fever in a village in which 21 out of 34 of the residents, living in a group of seven cottages built round a court containing a pump from a shallow well, were infected. They excreted Salmonella paratyphi B in their feces. That the outbreak was water borne was confirmed by the isolation of this organism from five different samples of the well water in three different laboratories. How the well became infected was not discovered, but there was ample opportunity for infection by pollution of the ground in the vicinity.

2:385-412 (Oct. 3) 1942

*Lid Retraction in Toxic Diffuse Goiter. K. C. Eden and W. R. Trotter. —p. 385.
Inguinal Hernia at Royal Air Force Hospital. H. R. Arthur.—p. 387.
Calcinosis Cutis and Scleroderma: Thibierge-Weissenbach Syndrome. E. W. P. Thomas.—p. 389.
*Absorption of Sulfanilamide Applied Locally: Blood Levels in Forty-One Cases. A. R. Hodgson and J. R. Robinson.—p. 392.
Juxtaglomerular Complex. J. F. A. McManus.—p. 394.
Potentialities of Municipal Medicine. H. Joules.—p. 396.
Advantages of a Socialized Medical Service. S. Hastings.—p. 397.

Lid Retraction in Toxic Diffuse Goiter.—Eden and Trotter state that lid retraction is, like exophthalmos, a characteristic feature of toxic diffuse goiter. The two conditions are easily separable clinically, though both give the impression of prominence of the eye. Lid retraction was present in 72 of 134 patients with toxic diffuse goiter, in 39 of whom it was associated with true or concealed exophthalmos. Unlike exophthalmos, which is apparently extrathyroid in origin, lid retraction usually disappears when the thyrotoxicosis becomes inactive, although occasionally it appears or persists in the absence of active thyrotoxicosis. Therefore lid retraction appears to be governed by two factors, one of which is derived from the thyroid and the other must come from another source (possibly the anterior pituitary gland).

Local Absorption of Sulfanilamide.—Hodgson and Robinson followed the sulfanilamide blood levels of 41 patients whose wounds, operative or others, were treated locally with the drug. Samples of blood for determination were taken every six or eight hours for the first twenty-four hours, then every twelve hours and finally daily. The value obtained twenty-four hours after operation was within 10 per cent of the peak value, except in 1 case, that of an arthroplasty of the hip. With this same exception the peak value was reached between sixteen and thirty hours after operation. In the case of the arthroplasty the blood sample taken eight hours after operation gave the highest concentration of sulfanilamide. The concentrations have usually been of the order of 1 mg. per hundred cubic centimeters of blood for each gram deposited in the wound. In many cases local application alone will maintain an adequate therapeutic level in the blood, so that simultaneous oral administration is by no means always necessary. When the tissue from which absorption occurs is muscle which has a good circulation, the blood concentration attained at the end of twenty-four hours per gram of drug deposited in the wound is in the neighborhood of unity. Indeed, with some wounds care is rather needed lest too much sulfanilamide be applied locally and toxic effects result from free absorption.

Medical Journal of Australia, Sydney

2:193-222 (Sept. 5) 1942

Shock and Anesthesia in Relation Thereto. A. D. Morgan.—p. 193.
Calculation of Heat and Moisture Dissipated from Body by Respiration, with Table Designed to Make Calculation Easy at Any Temperature, Any Humidity and Any Pressure of Air. C. E. Corlette.—p. 198.
Organization of Casualty Clearing Hospital for Air Raids. T. F. Rose.—p. 203.
Early Treatment of Battle Wounds of Head. D. Miller.—p. 207.

2:223-252 (Sept. 12) 1942

Dengue Fever. A. S. Walker, E. Meyers, A. R. Woodhill and R. N. McCulloch.—p. 223.
Active Immunization by Intranasal Route in Experimental Pertussis. E. A. North and G. Anderson.—p. 228.
Thiamine (Vitamine B_1) Content of Some Australian Biscuits and Breakfast Foods. E. C. Slater and Joan Rial.—p. 231.
Medical Conditions on Bathhurst and Melville Islands. E. Ford.—p. 235.
Besnier-Boeck-Schaumann Syndrome: Discussion, with Report of Two Cases. L. E. Hurley and J. F. Hughes.—p. 238.
Collodion Substitutes. H. L. Kesteven.—p. 240.

Schweizerische medizinische Wochenschrift, Basel

72:481-504 (May 2) 1942. **Partial Index**

Most Frequent and Important Abdominal Disorders in Children. E. Hagenbach.—p. 481.
*Lingual Application of Estradiol. K. Miescher and P. Gasche.—p. 490.
Possibility of Occurrence of Acute Gout Attacks in Disorders of Oxalic Acid Metabolism. J. Waclaw Grott.—p. 492.
Central Neurofibromatosis: Case. G. Piotrowski.—p. 495.

Lingual Application of Estradiol.—Having demonstrated that testosterone has a much more intensive action when administered by the lingual route, Miescher and Gasche investigated the effect of lingual administration of estradiol. The effect of the sublingual administration was compared with that of stomachal administration in a ten day test on 154 castrated female albino rats. In stomachal administration the drug was introduced by a stomach tube. In sublingual application drops were applied to the under surface of the tongue. It was found that alcoholic solutions of estradiol when administered by the lingual route exert an effect which is from ten to twenty times greater than that of stomachal administration. With the lingual administration effects can be obtained on the uterus which are not obtainable by stomachal administration. The estrus test likewise demonstrates a more intense action of the lingual administration. The uterus test, however, is much more sensitive than the estrus test. The efficacy of the lingual administration of estradiol is close to that of percutaneous or subcutaneous administration in the uterus test as well as in the estrus test.

Archivos de Pediatría del Uruguay, Montevideo

13:257-320 (May) 1942. **Partial Index**

*Shock Therapy in Typhoid Fever in Children. E. Peluffo and J. M. Portillo.—p. 257.

Shock Therapy in Typhoid Fever.—Peluffo and Portillo treated 65 children with typhoid fever with shock therapy induced by intravenous injection of antityphoid vaccine in hypertonic dextrose solution. The injections were made at intervals of two or three days. The first dose was 0.25 cc. of the vaccine, subsequent doses varied with the age of the patient from 1 to 1.5 cc. of the vaccine. Shock therapy by means of antityphoid vaccine had a favorable effect on the course of the disease in 50 per cent of the cases. The earlier the administration the better the results. Severe types of the disease were not influenced by this therapy.

Arch. Urug. de Med., Cir. y Especialid., Montevideo

19:561-652 (Dec.) 1941. **Partial Index**

Erythremia and Duodenal Ulcer: Efficacy of Teleroentgen Therapy. B. Varela Fuentes, R. Canzani and A. Frangella.—p. 561.
*Pulmonary Complications of Diphtheria in Adults. E. M. Claveaux and F. J. Salveraglio.—p. 582.
Sedimentation Speed of Erythrocytes in Typhoid. R. Piaggio Blanco and C. M. Sanguinetti.—p. 587.
*Pigmented Spots on Face Cured by Injection and Local Application of Folliculin. F. Rocca.—p. 592.

Pulmonary Complications of Diphtheria in Adults.—According to Claveaux and Salveraglio, pulmonary complications of diphtheria in adults have received little attention although they prove fatal in the majority of the cases. The mode of origin and its significance vary according to the time of appearance of the pneumonic process. There is a type of a lesion seen in the course of an extensive laryngotracheobronchial diphtheria. Formation of intrabronchial pseudomembranes produces obstruction of the bronchi, which in turn leads to formation of foci of atelectasis which become rapidly infected and give rise to secondary bronchopneumonia. The authors had the opportunity of studying several of these extensive cases of diphtheria in adults. Signs of diffuse bronchitis with dyspnea and cyanosis are the usual clinical symptoms. Roentgenologic examination reveals multiple pulmonary shadows. Anatomicopathologic study discloses involvement of the entire bronchial tree by pseudomembranes, multiple foci of bronchopneumonia and atelectasis. Another type of lesion is represented by the bronchopneumonia of croup. This is seen more often in children. The authors observed it in a patient aged 21 who on the day after having undergone tracheotomy for croup developed a severe bronchopneumonia which terminated in cure. The pulmonary congestion produced by the diphtheritic toxin, the impairment of the pulmonary ventilation due to laryngeal stenosis and bronchial obstruction by pieces of pseudomembrane and aspiration of blood after tracheotomy are the factors which cause this bronchopneumonia. Acute pulmonary processes in the course of the secondary syndrome and of diphtheritic paralysis represent a special type. Paralysis of the muscles of respiration is the factor chiefly responsible for this form. Paralysis and anesthesia of the larynx make possible the passage of food into the respiratory passages and thus contribute to the production of septic pulmonary processes. These lesions are nearly always fatal. Paralysis of the respiratory muscles is an obstacle to successful treatment in these cases. However, prophylactic treatment can be effective in preventing these complications. The authors recommend careful disinfection of the upper air passages and frequent inhalations of oxygen alternating with carbon dioxide-oxygen mixture. To avoid the passage of food into the air passages in the presence of the paralysis of the muscles of the throat it is advisable to feed the patients by rectum, by the subcutaneous route or by the nasal tube.

Estrone in Treatment of Pigmented Spots.—Rocca tells of a woman of menopausal age who developed coffee colored spots on the face, particularly about the eyes, in the ciliary and supraciliary region, on the cheek bones and on the arms and knees. Microscopic examination of an excised spot from the arm indicated that they were not pigmented nevi. Disturbances in pigmentation frequently result from endocrine disturbances of the menopause, although they are rarely as severe as in the case cited here. Twice a week, for a period of several months, 5,000 international units of estrone was administered by injection. The menstrual disturbances became regulated, the subjective symptoms improved and the facial spots began to clear up. An estrone ointment was now applied to the facial spots for twenty days. It was observed that some spots disappeared and others became much lighter. Local and injection treatments were continued for several months, when the pigmentation had decreased greatly on the face and in many parts of the body. When the endocrine treatment had been interrupted for a year, small spots began to appear in the ciliary region.

Revista de Cirugía de Buenos Aires

21:121-178 (April) 1942. **Partial Index**

*Perforating Posterior Fornical Endometriosis: Cases. J. C. Ahumada, J. A. Salaber and A. E. Nogués.—p. 121.
Idiopathic Diverticula of Duodenum. M. S. Guitarte.—p. 135.
Subarachnoid Meningocele of Sacral Region. A. Gutiérrez.—p. 156.

Endometriosis.—According to Ahumada and collaborators perforating posterior endometriosis is rare. It is more frequent in young women. Symptoms, as a rule, are the same as in pelvic endometriosis. Small, acyclic, intermenstrual metrorrhagia, pressure on the rectum, or stenosis of same, are the most frequent symptoms. A characteristic finding during gynecologic examination is a hard nodule located behind the cervix, extending laterally and infiltrating the parametrial tissue and the uterosacral ligaments. The tumor may invade the rectal wall. In the early stages the vaginal mucosa is hard, inelastic and congested. In the advanced phase a more or less large

tumor or a polypoid formation on a hard neoplastic base is present. Diagnosis in the early and late stages is difficult. The clinical history of the patient, changes in the tumor during menstruation and aggravation of the symptoms during menstruation are suggestive. The diagnosis is verified by biopsy. Surgical therapy varies with the stage of the disease. In the early stage the operation consists of a total removal of the endometriosic plate through a median laparotomy with a subtotal hysterectomy and bilateral salpingectomy. Surgical castration is indicated in advanced cases and roentgenologic castration in the far advanced cases.

Revista Clínica Española, Madrid

4:161-232 (Feb. 15) 1942. **Partial Index**

Tuberculous Superinfection and Reinfection in Adult: Present Status of Problem. A. Urgoiti and J. L. Alvarez-Sala.—p. 161.
*Panmyelophthisis Following Arsphenamine Therapy of Syphilis: Case. J. Rof Carballo and J. Parras Benito.—p. 167.
Experimental Investigations in a Case of Solar Urticaria. J. Gay Prieto, J. M. López de Azcona, L. Azúa, F. Bondeu and M. Cárdenas.—p. 173.
Metabolic Craniopathy. C. Jiménez-Díaz, J. Rof, A. Romero and L. Lara.—p. 178.
Colloidoclastic Reaction of Mester in Differential Diagnosis of Rheumatic Disease. T. Cerviá and J. García López.—p. 183..
Arthrodesis with Flexible Graft for Treatment of Tuberculosis of Elbow. J. Gascó Pascual.—p. 186.
*Plasma Transfusions in Therapy of Hepatic Cirrhosis. C. Jiménez-Díaz, E. Roda, F. López Ruiz and P. Breñas.—p. 191.
Jaundice Due to Atophan (Cinchophen): Two New Cases. A. Romero Calatayud.—p. 196.

Panmyelophthisis Following Arsphenamine Therapy.—Rof Carballo and Parras Benito report a case of aplastic anemia with leukopenia and granulocytopenia as well as with hemorrhagic diathesis following combined arsphenamine and bismuth therapy. The extremely grave condition improved following repeated small blood transfusions. During the period of severest anemia, puncture of the bone marrow yielded only fat, but during recuperation it was slowly transformed again into normal bone marrow. The clinical improvement was indicated in advance by an increase in monocytes in the peripheral blood. The good result of the treatment in the extremely severe case indicates that small blood transfusions should be given repeatedly, particularly in cases of aplastic anemia or panmyelophthisis, in which the presence of monocytes indicates that the prognosis is not entirely hopeless. Even if puncture of the bone marrow repeatedly shows its total aplasia, this does not justify the neglect of an energetic stimulation of the hemopoietic organs.

Plasma Transfusion in Hepatic Cirrhosis.—Jiménez-Díaz and his associates demonstrated in 1929 that in experimental hepatic disorders produced by chloroform the alteration of the hepatic parenchyma was accompanied by a diminished protein content of the plasma and by albumin-globulin inversion. Wallich demonstrated an identical disturbance. The authors investigated the effect of the administration of different types of albumin on hepatic cirrhosis. Intravenous injection of plasma proteins rapidly restored the total protein content of patients with hepatic cirrhosis. The efficacy of mercurial preparations is enhanced, and even without these the diuresis is improved. The development of ascites is arrested, and in 1 patient reabsorption was obtained.

4:393-468 (March 30) 1942. **Partial Index**

Lipoid Metabolism; Relation of Hyperlipemia Due to Obstruction of Choledochus to Abscence of Bile in Intestine. C. Jiménez-Diaz and H. Castro-Mendoza.—p. 398.
Immediate Postoperative Results in Biliary Surgery. J. Pi-Figueras, V. Artigas, A. Gallart-Esquerdo and E. Sierra.—p. 403.
*Casal's Disease: Roentgen Behavior of Stomach in Pellagra. M. Diaz-Rubio and L. Lara Roldán.—p. 408.
Attempted Sulfanilamide Therapy in Malaria. R. Diaz Mora.—p. 413.
Supernumerary Bones: Superior Cotyloid Bone, Os Trigonum, Peroneum and Anterior Tibial Bone. V. Sanchis-Olmos.—p. 419.
*Sulfapyridine Therapy of Persistent Bacterial Asthmas. C. Jiménez-Diaz, C. Lahoz and L. Recatero.—p. 423.
First Case of Cooley's Anemia in Spain. E. Jaso, J. M. Alés Reinlein and J. Pardo Urdapilleta.—p. 425.

Stomach in Pellagra.—Díaz-Rubio and Lara Roldán made roentgenologic studies of the stomach in 255 patients with pellagra. Most noteworthy feature was diminution of gastric peristalsis which often gave rise to great dilatation and retarded evacuation of stomach contents. The mucosa was atrophic in over 67 per cent of the cases. The atrophy was diffuse in the majority of the cases and limited to certain zones in 16 per cent. A number of patients presented intense aerogastria and a few had large amounts of mucus. In 22.35 per cent of the cases roentgenologic appearances of the stomach were normal as regards the tonus, peristalsis, evacuation and relief of the mucosa, in spite of the fact that pellagra was fully developed. There were some cases in which no relationship existed between the severity of the changes and the gravity of the clinical picture, but in 59 patients, on whom at least 3 studies were made, there was a close parallelism between the clinical picture and the intensity of the radiologic signs. Roentgenologic examination of the intestine disclosed severe aerocoly, inflammation of the large intestine and retention of the contrast meal in the terminal loops of the ileum. Comparison of the roentgenologic appearance of the gastric mucosa of these patients with those of achylia, suggests that the organic changes in the mucosa are sequels to the functional disturbances.

Sulfapyridine in Asthma.—From observation and experimental studies Jiménez-Díaz and his collaborators gained the impression that bacterial infection plays a part in some cases of bronchial asthma. Ten patients with true "status asthmaticus," who for months had proved refractory to various methods of treatment, were given sulfapyridine. In 8 of these, this therapy effected the disappearance of all symptoms; in 2 the drug was without effect.

Revista de Neuro-Psiquiatría, Lima

5:137-314 (June) 1942. **Partial Index**

Evolution of Neurologic Thought in Neurobiology. J. O. Trelles.—p. 137.
*Cerebral Tuberculosis. J. Voto-Bernales.—p. 165.

Cerebral Tuberculosis.—Voto-Bernales found in a study of 22 cases of brain tuberculosis that the process is always secondary to tuberculosis elsewhere. The method of dissemination is most likely the hematogenous. Tuberculoma, tuberculous encephalitis and especially tuberculous meningitis are the main terminal clinical types of the disease. Tuberculosis with symptoms of epilepsy and of mixed forms of the disease are terminal clinical types less frequently seen than the foregoing. In many cases the disease develops without symptoms. The diagnosis of asymptomatic types is difficult. It is based mainly on the existence of tuberculosis elsewhere. Cerebral tuberculosis pursues a slow progressive course and leads to grave symptoms. Spontaneous recovery is extremely rare. There is neither a proper medical nor surgical therapy for the disease. The treatment consists in general care of a tuberculous patient and in decompression by trephining when indicated.

Archiv für Gewerbepathologie, Berlin

10:445-568 (April 16) 1942. **Partial Index**

*Lesions Produced by Light Metals. E. Sedlacek.—p. 445.
Fatal Poisoning with Chlorosulfonic Acid. F. Roulet and O. Straub.—p. 451.
*Electron Microscopy on Asbestos Dust and on Lungs in Asbestosis. J. Kühn.—p. 473.
Occupational Injuries Caused by Radiant Heat in Rolling Mills: Development of Skin Cancer. H. Waniek.—p. 486.
*Silicosis of Intrathoracic Lymph Nodes as Compensable Occupational Disease. J. Hagen.—p. 502.
Siderosis of Lungs in Electric Welders. F. Koelsch.—p. 519.
Lesions Caused by Light Metals. W. Hofbauer.—p. 529.
*Spinal Cord and Peripheral Nervous System in Chronic Manganese Poisoning: Pathologic Anatomy of Manganism. H. Voss.—p. 550.

Lesions Produced by Light Metals.—As a physician in an airplane factory Sedlacek frequently encountered inflammations following cut injuries with duraluminum. These inflammations are mostly seen in wounds too small for surgical care. Large wounds caused by duraluminum are excised and sutured. Subsequent inflammations are rare. The appearance of a blister filled with serous fluid is characteristic of an unexcised duraluminum lesion. The blister is usually in evidence from one to two days after the injury. The contents of the blister suppurate, and in some cases necrosis develops at the base. The inflammation spreads to the surrounding tissues, and a lymph-

angitis or a lymphadenitis may develop. In addition to dermatitis, conjunctivitis and gastritis may develop. These lesions can be explained by the mechanical action of duraluminum dust, which develops in the course of drilling, can be inhaled or swallowed and, although extremely fine, may cause epithelial defects in the mucosa. Allergy does not play a part, because cutaneous tests were always negative and the blood tests made by Utz failed as a rule to disclose eosinophilia.

Electron Microscopy in Asbestosis.—Kühn says that because the asbestos used in factories is mostly serpentine (chrysotile) asbestos and not so much hornblende asbestos, it was generally believed that the asbestos substance found in lungs with asbestosis is chiefly serpentine asbestos. Studies by Sundius and Bygdén disclosed, however, that only hornblende asbestos is demonstrable in the lungs, which seems to suggest that serpentine dust is decomposed in the tissues. Kühn used the electron microscope to study form, size and structure of asbestos dust and the asbestos found in the lungs. It was possible to detect a considerable number of asbestos dust particles that were below the threshold of the ordinary microscope. The needles of chrysotile asbestos appear under the electron microscope curved, clear and transparent. The needles of hornblende asbestos are rigid, and curved pieces are rare; their diameter is usually greater than that of serpentine (chrysotile) asbestos. Needles were isolated from 3 lungs with asbestosis. Their examination under the electron microscope disclosed size and form but did not aid in deciding whether the asbestos was chiefly of the serpentine or of the hornblende type. For this reason it was decided to employ the photomicroscopic determination of the refraction exponent as suggested by Sundius and Bygdén. This method revealed that the large asbestos needles isolated from the lungs were of the hornblende type. It is concluded that serpentine asbestos is decomposed in the lungs and is the essential cause of fibrosis. If asbestosis lungs are macerated with nitric acid and hydrogen peroxide, not only are free asbestos needles obtained but also asbestosis bodies. Hornblende asbestos shows no signs of decomposition by the organism either in the free needles or on the asbestosis bodies.

Silicosis of Intrathoracic Lymph Nodes.—According to Hagen, reports on silicosis as well as the legal regulation concerning compensation for occupational disease are concerned chiefly with silicotic changes in the pulmonary tissue. He describes several cases of complicating severe silicosis of the intrathoracic lymph nodes with a fatal outcome. The first patient, a man aged 63, had comparatively slight silicotic changes in the lungs, but there existed a severe silicosis of the lymph nodes at the bifurcation, which by severe cicatricial shrinkage led to the formation of 3 traction diverticula in the esophagus. Perforation of a diverticulum led to pulmonary abscess formation, bronchiectasis and generalized suppurative bronchitis. The fatal outcome of the pulmonary abscesses must be regarded as the result of silicosis. Several additional cases are described and evaluated and the conclusion is reached that silicosis of the lymph nodes, if it becomes the point of origin of a severe disorder, must be regarded as a compensable disorder, just as severe silicosis of the pulmonary tissue.

Nervous System in Manganese Poisoning.—Voss maintains that the anatomic basis of manganese poisoning has not been clarified. Neither the few histopathologic studies on human subjects nor animal experiments have given reliable results. Changes regarded as specific for manganese poisoning could be explained also as the result of complicating disease or as caused by the age of the patient. The assumption that the clinical manifestations of manganism are due chiefly to extrapyramidal motor lesions, particularly an impairment of the pallidum, has not been definitely corroborated by anatomic findings. In view of the fact that the clinical symptoms of manganism resemble those of paralysis agitans and postencephalitic parkinsonism, changes could be expected in the substantia nigra. However, this region was found completely intact, not only by earlier investigators, but also by the author, who studied this region in 2 cases. Examination of the spinal cord and peripheral nerves of patients with manganese poisoning has been largely neglected hitherto. Whereas in the 2 cases reviewed by the author the brain was found to be practically normal, important changes were seen in the spinal cord and in the peripheral nervous system. In one of the patients the manganese poisoning had taken an atypical course. Amyotrophic lateral sclerosis with bulbar symptoms dominated the clinical picture, and anatomic studies disclosed corresponding changes. The second case presented classic symptoms of manganism. As is frequently observed in manganese poisoning, certain pyramidal symptoms were present, but changes in the peripheral nerves were not to be suspected. Anatomic studies disclosed extensive degeneration in the right lateral pyramidal tract and in both sciatic nerves with pronounced vascular disturbances in the diseased regions. Other nerves had not been examined. The author is convinced that manganese poisoning was the cause or at least a contributing factor of the described changes. Studies should be made not only of the brain but of the spinal cord and the peripheral nerves as well.

Archiv für Kreislaufforschung, Dresden

9:123-302 (Oct.) 1941. **Partial Index**

Cardiac Pains and Electrocardiographic Aspects: Relations to Anoxia. H. Oettel.—p. 123.
*Seasonal Changes in Some Circulatory Factors. H. Paul.—p. 164.
Muscular Tonus and Its Relations to Peripheral Circulation. G. Budelmann.—p. 188.
*Influence of Increased Thyroid Activity on Altitude Tolerance in Animal Experiments. W. Rotter.—p. 226.
Syphilis of Aorta: Changes in Frequency and Symptomatology During Last 20 Years. H. Deitert.—p. 258.

Seasonal Changes in Circulatory Factors.—Paul studied seasonal changes in the pulse frequency, in the blood pressure at rest and after exertion, in the values derived therefrom and in the vital capacity on 900 healthy men between the ages of 17 and 30. The pulse rate during rest, as well as after exertion, showed noticeable seasonal changes. The maximum was observed during the winter months, January to March; the minimum during the summer months July to September. Seasonal fluctuations in the blood pressure could not be clearly established. The product of amplitude and frequency, in spite of considerable scattering of individual values, clearly showed an annual curve; the maximum is in March, the minimum in September. However, no seasonal fluctuations could be detected in the exertion values. The vital capacity shows an extremely low minimum in June.

Increased Thyroid Activity and Altitude Tolerance.—Rotter made animal experiments to determine whether increased thyroid function would modify altitude tolerance. He treated guinea pigs with thyrotropic hormone so as to increase the thyroid function and to intensify tissue combustion. These animals, together with normal controls, were subjected to short term experiments in the low pressure chamber. It was observed that the animals which had been treated with thyroid had respiratory arrest at a time when the untreated animals still felt comparatively well. Comparative electrocardiographic tests, made at intervals, disclosed that the hearts of the guinea pigs which had been pretreated with thyroid were much more vulnerable to oxygen deficiency than those of the untreated controls. The pretreated animals showed during the experiment a greatly increased sympathetic tonus. Microscopic examination of the organs, however, permitted no conclusions regarding the greater sensitivity to oxygen deficiency of the pretreated in comparison with the untreated animals.

Medizinische Klinik, Berlin

37:1097-1120 (Oct. 31) 1941. **Partial Index**

Diagnosis of Cutaneous Diseases in Various Regions of the Body. W. Krantz.—p. 1097.
*Spontaneous Desensitization in Occupational Eczema and Its Significance for Estimation. F. Koch.—p. 1100.
Aspects of Pneumococcic Peritonitis. M. Krabbel.—p. 1105.
Treatment of Fracture of Neck of Femur in the Aged. H. Tammann.—p. 1106.
Question of Themostability of Botulinus Toxin. P. Dahr.—p. 1107.

Spontaneous Desensitization in Occupational Eczema.—Koch states that follow-up examinations on patients with occupational eczema who had been advised to change their occupation revealed that many had not followed the advice. The majority of the patients remained subject to eczema, but

some had lost it in spite of further contact. Of 131 patients, 20 showed this contradictory behavior. Among the 60 bakers who were reexamined there were 10 in whom the eczema had disappeared and among the 71 persons of other occupations there were likewise 10. The explanation of such spontaneous cures and the underlying processes are of considerable interest. Regular weekly observations on 8 patients disclosed two different forms of development. One group of 5 patients experienced at every resumption of work first a considerable exacerbation of the disorder, usually with the aspects of an acute eczema, with considerable inflammation and itching. However, in spite of continuing the work there now followed, in contradistinction to earlier attacks, a gradual regression of the manifestations, which finally resulted in a complete or an almost complete disappearance of the eczema. Small foci recurred occasionally, but these could be controlled with simple measures. They did not necessitate the interruption of the occupation. However, when work was resumed after it had been interrupted for a while on account of holidays, vacations or layoff, there was a renewed exacerbation, which, however, was followed by almost complete freedom from complaints. The course in the 3 other cases was somewhat different. In these too the eczema recurred on the hands when work was resumed, that is, at the sites where it had been originally and which were chiefly exposed to the offensive substances. Later the lesion on the hands healed and recurred at other sites of the body, in 1 case at the border of the original eczema, which now had disappeared. The recurrence was so mild that the working capacity was not impaired. The author thinks that the only possible explanation is a desensitization, which presupposes specific allergic processes. He explains the difficulties encountered if an explanation is attempted and believes that eczema is not a pathogenic unit. Various other factors besides the allergic may play a part. Results of artificial desensitization carried out for therapeutic purposes have been slight. This therapeutic method cannot be generally recommended, but it should not be completely abandoned. Further observations may disclose regularities which may become the basis for more favorable results.

Zeitschrift f. d. ges. experimentelle Medizin, Berlin

108:531-666 (March 3) 1941. **Partial Index**

Changes in Pulse Frequency During Controlled Ergometric Work. D. Albers.—p. 531.
Passage of Prontosil and Other Dyes from Blood Stream into Pleural Exudates and in Reversed Direction. H. Bauer.—p. 537.
Combined Antitrypsin Method for Differential Diagnosis of Tumors and Infections. H. Kämmerer and W. Bruckmeier.—p. 551.
Weakening and Abolishment of Vasoconstricting Effect of Epinephrine in Skin. J. Frey and H. Horn.—p. 567.
Ascorbic Acid and Schultz-Dale Phenomenon. C. Bembé.—p. 581.
*Physiologic and Chemical Studies on Patients with Latent Allergy as Contribution to Problem of Allergic Constitution. G. Albus.—p. 592.

Physiologic and Chemical Studies in Latent Allergy.—According to Albus the basis of allergy is not purely serologic but the still largely unknown process in the body cells which is probably more of a physiologic or pharmacologic nature. The author describes physiologic and chemical studies on nonallergic persons and patients with latent allergy. The latter were clinically healthy persons with a history of allergy. The studies concerned serum protein, serum globulins, serum calcium, blood sugar, serum cholesterol, histaminase and acetylcholine esterase. It was found that as regards serum protein, serum calcium and blood sugar there was no difference between nonallergic and allergic persons. The globulins seem to be increased in allergic persons. It is suspected that the cholesterol ester is reduced in the serum of allergic patients. The activity of histaminase and choline esterase of the blood is noticeably decreased in allergic patients. The author discusses sensitization, antigen antibody reaction, histamine and histaminase, development of allergic reactions, secondary effects of allergic reactions and the allergic constitution and its modification. He sets forth the hypothesis that the allergen resorption as well as the antigen antibody reaction are for every individual continuously evolving normal physiologic processes. The person with an allergic constitution, because of the reduced activity of his histaminase and choline esterase has an increased susceptibility to histamine and acetylcholine. It is suggested that the more comprehensive term "histamine-susceptible constitution" be substituted for "allergic constitution." There are still problems that require investigation, such as the role of epinephrine oxydase in allergy. Experimental studies demonstrated that the increase in serum globulins in allergic persons is due to their increased concentration gradient for histamine, because in animal experiments sensitization and frequent small doses of histamine effect a noticeable increase in serum globulins; in tests on human subjects glutathione, ascorbic acid and thiosulfate produce reduction in the serum globulins. The author denies that a colloidoclastic crisis is a prerequisite for the development of an allergic reaction. He suggests that insufficient negativity of the redox potential is the deeper cause of the histamine susceptible constitution. Administration of large quantities of vitamin C does not seem to solve the problem of treatment in allergy. The cardinal problem is how the organism can be influenced to retain and properly utilize the redox substances. A blood transfusion has been known to improve the storage capacity for vitamin C in a case in which vitamin therapy had been a failure previously. Although there is as yet insufficient evidence for the administration of redox substances, it is essential to keep away from the allergic patient all substances that impair the redox potential.

Zeitschrift für Immunitätsforschung, Jena

99:257-332 (Feb. 20) 1941. **Partial Index**

*Question of Relationship Between Sensitivity to Odor of Horses and Horse Serum Hypersensitivity. W. Hartmann.—p. 257.
Mode of Action of Antibacteriophage Serum and of Tannic Acid on Bacteriophage Protein. H. Moriyama and S. Ohashi.—p. 282.
Experiences with Dry Blood Reaction, Meinicke Clarification Reaction II, for Syphilis According to Meinicke and Fischer. D. Gigante.—p. 299.
Consideration of Problems Connected with Pathogenesis of Diphtheria. A. Zironi.—p. 309.
Leptospirosis in Tame Laboratory Rats and Immunization of Personnel Exposed to Infection. W. Schüffner.—p. 323.

Sensitivity to Odor of Horses and Horse Serum Hypersensitivity.—Hartmann investigated the question of a relationship between sensitivity to the odor of horses and hypersensitivity to horse serum. He inquired of 1,668 persons (1) whether they were sensitive to the odor of horses, (2) whether they ever received an injection of horse serum and (3) whether, in doing so, they developed signs of serum disease. The group included men in military hospitals and men, women and children in a city hospital varying in ages between 5 and 65 years. The inquiry disclosed that 26, or 1.55 per cent, were sensitive to the odor of horses. Of the 26, 7 had previously been treated with horse serum and none had had signs of serum disease. Only 1 of 17 persons sensitive to horse odor given an intracutaneous injection of 0.1 cc. of horse serum developed a mild local reaction, and this person had received tetanus serum one month previously. Of the 1,647 persons who were not sensitive to the odor of horses 171 had been treated once with horse serum, and of these 16 had had signs of serum disease. The intracutaneous injection of 0.1 cc. of horse serum into 10 persons not sensitive to the odor of horses, but previously treated with horse serum, without showing signs of serum disease, resulted in a local reaction in only 1. Ten children not sensitive to the odor of horses, but who had been treated from three to five weeks previously with diphtheria or scarlet fever horse serum, were also given an intracutaneous injection of 0.1 cc. of horse serum. Among these there were 4 who showed a mild reaction around the site of injection. It was thus impossible to establish a relationship between sensitivity to the odor of horses and hypersensitivity to horse serum. Testing fluids were extracted from the urine, sweat and cutaneous scales of horses, and these were used for intracutaneous tests on persons sensitive and not sensitive to the odor of horses. These tests again failed to reveal a relationship between the sensitivity to the odor of horses and to the aforementioned extracts. Eating of horse meat caused no reactions in 2 persons who were sensitive to the odor of horses. The author concluded that there is no connection between sensitivity to horse odor and hypersensitivity to horse serum.

Book Notices

The Pathology of Trauma. By Alan Richards Moritz, M.D., Professor of Legal Medicine, Harvard Medical School, Boston. Cloth. Price, $6. Pp. 386, with 117 illustrations. Philadelphia: Lea & Febiger, 1942.

The purpose of the author is to compile a volume which is primarily devoted to the pathogenesis, pathologic anatomy and histology of traumatic lesions which have not hitherto been adequately treated in the literature. Topics which have been satisfactorily considered are discussed briefly in the interest of completeness. The general plan of the book is satisfactory, the chapter arrangement beginning with a general consideration of mechanical injuries including various types of trauma: gunshot wounds, stab wounds and injuries due to blunt force. Other sections are devoted to trauma and infection, trauma and tumor and then follows a discussion of the lesions of the various body systems, special organs and tissues, their complications and sequelae. Attention has been given to controversial questions, notably in the chapter on trauma and tumors and in the discussion of the productive mechanism of cerebral concussion, and Moritz's reasoning is in agreement with generally accepted opinions. To those who are unfamiliar with recent advances in forensic investigations the information on the various laboratory procedures for testing discharged powder residues on the skin and clothing in gunshot wounds, the use of infra-red photography in the examination of the clothes in these cases and the utilization of ultraviolet rays in other investigations may be of interest. The section on injuries resulting from detonation of high explosives is also particularly pertinent at this time. Many other parts of the book are informative, especially the discussion of the exacerbation of diseases by trauma and the section on asphyxia of traumatic origin. Adequate references are given for those who wish to pursue further the topics which are under discussion. The illustrations are excellent and clearly depict the points which the author wishes to emphasize and are conveniently located in relation to the text. While there are a few minor omissions and the index could be improved on, generally considered the book will be a valuable addition to the library of the student of forensic medicine as well as of clinicians and pathologists, for whom the book is intended. Incidentally it collects in one handy and convenient volume much information which would otherwise necessitate an exhaustive search of the literature.

Food Charts: Foods as Sources of the Dietary Essentials. Prepared by a Joint Committee of the Council on Foods and Nutrition of the American Medical Association and of the Food and Nutrition Board of the National Research Council. Paper. Price, 10 cents: quantity prices on request. Pp. 20. Chicago: American Medical Association, 1942.

This well illustrated essay is an interesting and forceful presentation of some of the recently acquired quantitative information about foods as sources of the dietary essentials. It has been prepared by a joint committee of the Council on Foods and Nutrition of the American Medical Association and of the Food and Nutrition Board of the National Research Council. There are eight charts which show the contribution of individual foods to the needs for protein, calcium, iron, vitamin A, thiamine, riboflavin, nicotinic acid and ascorbic acid. A feature of these graphic presentations is that the values are presented in terms of the percentage of the daily requirements which are supplied by typical servings of each food. The requirements selected are the Recommended Daily Allowances of the Food and Nutrition Board of the National Research Council. The charts show, for example, that a serving of about 3½ ounces of cooked greens (beet, kale, chard, mustard, spinach, turnip) will supply more than 10,000 international units of provitamin A, the daily allowance of which is 5,000 international units. An orange of average size, half a grapefruit or a serving of fresh strawberries will supply the 75 mg. of ascorbic acid which is considered to be a desirable intake of vitamin C. It is interesting to note the unique value of milk as a source of calcium, protein and riboflavin. There is a descriptive paragraph or two about each of the charts. In addition the booklet reproduces the table of Recommended Dietary Allowances and also provides the values of Minimum Dietary Requirements developed by the Food and Drug Administration for purposes of labeling special dietary foods. This little booklet thus provides a considerable amount of information about foods.

History of the School of Nursing of the Presbyterian Hospital, New York, 1892-1942. By Eleanor Lee, A.B., R.N., Assistant Professor of Nursing, Department of Nursing, College of Physicians and Surgeons, Columbia University, New York. Cloth. Price, $3.50. Pp. 286, with 57 illustrations. New York: G. P. Putnam's Sons, 1942.

Rarely does one find a volume so free from flaw as this one by Miss Eleanor Lee. Her knowledge of the Presbyterian Hospital, coupled with her being well versed in the history of nursing, makes her especially qualified for just such a work as this. That she has done it with real skill is revealed through the contents, with ten chapters, over fifty illustrations, a chronological list of events from 1892 to June 1942, an appendix, pages of which are original copies in facsimile; junior and senior lectures, 1893-1894; graduating exercises of the class of 1894 in the Training School for Nurses, with notes from diaries of members; the history and significance of the Presbyterian nurse's pin; speakers at graduation, 1894-1942; presidents of the alumnae association; a prayer offered at the funeral of Miss Maxwell; Presbyterian Hospital School of Nursing Hymn; hospital officers administrative staff, nursing service; Faculty of Medicine of the College of Physicians and Surgeons; officers of instruction, Department of Nursing; plan of instruction, 1942; explanation of table of trends in nursing; bibliography, and a helpful index.

To select one feature as most prominent is difficult, but through the table of contents one sees what ground is covered, and one needs only to go through these chapters to see how great a piece of work this has been, with method most meticulous, attention to minute details and throughness by the author, all of which make the volume increasingly valuable with all its information and also as a tool of reference. Each chapter has its own part in forming the whole, many having worthily contributed toward making the volume all that it is, and, where mention can not be made in the contents, mention is made in the index, as in the case of the Florence Nightingale Memorabilia, easily beyond compare and as delightful in its way as is the chapter on the Alumnae Association.

Chapter I is chiefly devoted to the Presbyterian Hospital in its early days at the time of its opening on Oct. 10, 1872 and, as its title implies, the Presbyterian Hospital before the establishment of the Training School for Nurses. Mention is made of its benefactors and various organizations, how middle aged women were employed as nurses, with their training gained through experience and with the help of doctors, up to 1891, when, because of increased demands on the hospital, and, in awareness of the great possibilities the work of nursing might extend, decision was made to establish its own training school.

With chapter II, on the founding and early development of the Training School for Nurses, the Training School for Nurses was opened in May 1892, Miss Anna Caroline Maxwell having taken over her duties as superintendent of nurses on January 1 of that year. From the time of her appointment until her retirement in June 1921, constant progress was made through the untiring and devoted service of this gifted woman, all of which has been ably continued by Miss Helen Young, acting director at the time of Miss Maxwell's retirement, who was made director of the Nursing Service and the School of Nursing of the Presbyterian Hospital in 1923.

To both of these praiseworthy women the author has given high merit, as well as to others where merit was due, thus reflecting merit on herself, equally deserved. From the time the Training School for Nurses was born, all worked loyally, perhaps little dreaming on "how firm a foundation"—toward what has now become the Department of Nursing of the College of Physicians and Surgeons, Presbyterian Hospital School of Nursing,—a monument of service to serve all "without regard to race, creed or color." Credit should also go to the publishers, who have done fine work with their neat binding, paper, print and entire format, adding their part to a work already easily readable. It is a volume that should find an early place not only in all medical and hospital libraries, but in public libraries as well, as also in the hands of doctors and countless lay readers, for all of whom it will arouse interest in history not yet awakened and stimulate that already alive in the many who long since have learned the joy of all that is historical.

Massage, Manipulation and Local Anaesthesia. By James Cyriax, M.D., B.Ch., Assistant Medical Officer, Physiotherapeutic Department, St. Thomas's Hospital, London. Cloth. Price, 12s. 6d. Pp. 302, with 26 illustrations. London: Hamish Hamilton Medical Books, 1941.

This monograph opens with the statement that "this work is intended primarily for graduate masseuses and for the medical practitioners from whom they receive instructions." In the United States most medical men instructing physical therapy technicians would not recommend the book to their students because many of the procedures described have never before been published and many of the technics presented would have to be verified by a physician before he could recommend them.

Among the many subjects dealt with for the first time, attention may be drawn to the author's technic for the treatment of spastic conditions of the alimentary tract by manipulation of the intestine. The author believes that great improvement, even cure of long standing abdominal disorders, can be achieved by manual treatment of the gastrointestinal tract. Considerable experience and the use of controls will be required to substantiate the author's statements "Paradoxically enough, constipation is harmless as long as no effort is made to treat it by taking laxative medicines" and "If the perineum is lax, the tone of the levator ani muscle can be restored by active exercises even years after childbirth." Cyriac outlines the material on a regional basis and gives the conditions in each region that are amenable to the application of physical therapy. His theories have been evolved over a period of years in the course of a systematic reevaluation of long established methods. Their advantages have been amply demonstrated to the author and his colleagues in the physical therapy department of St. Thomas's Hospital. His approach to the subject matter is practical. Although the book is thought provoking the theories presented will need further investigation, especially by physical therapy physicians.

Los Angeles County Hospital, House Staff Manual. Edited by Morris F. Collen, M.D. Third edition. Paper. Price, $3. Pp. 342, with 1 illustration. Los Angeles, 1942.

This manual, prepared for the guidance of the house staff of the Los Angeles County Hospital, has been completely revised since the publication of the second edition in 1941. It is abreast of modern practice and is sufficiently comprehensive to cover the essential needs in relation to general rules and regulations, minor technical procedures, the hospital formulary, diet outlines, laboratory procedures and other departmental routines. These standardized procedures should prove exceedingly helpful to new house officers, who must necessarily consolidate and systematize their knowledge in order to function efficiently in a complex hospital organization. Directive outlines are included with reference to physical therapy, radiation therapy, general medicine, contagious diseases, pediatrics, neuromedicine, neurosurgery, general surgery, anesthesia, urology, orthopedics, fractures, gynecology, obstetrics, dermatology-syphilology, ophthalmology and otolaryngology. There are special sections on sulfonamide therapy, war gases, burns, immunization procedures, public health regulations and psychiatric studies. Full directions of diagnostic and therapeutic methods are included in all outlines. The present volume can be highly recommended as a model for other hospitals seeking to develop a suitable "procedure book" for their own needs.

Emergency Care. By Marie A. Wooders, B.S., R.N., Principal, School of Nursing, Hackensack Hospital, Hackensack, N. J., and Donald A. Curtis, M.D., Lieutenant Colonel, Medical Reserve, Commanding 342d Medical Regiment, United States Army, Hackensack. Cloth. Price, $3.50. Pp. 560, with 201 illustrations. Philadelphia: F. A. Davis Company, 1942.

The title of this book implies correctly that it is more than just another manual on first aid. Col. Walter P. Davenport states in a foreword that in addition to fulfilling its purpose as a nurses' manual for service in national and civilian emergencies it will prove of assistance to nurses in their professional duties and will orient them in the realities of nursing as modified by the necessities of military service. The book is divided into sections devoted to general emergencies, hospital accidents, accidents due to individual activities—home and farm accidents—occupational emergencies—camp, school and industry—public emergencies (major disasters) and national and civil emergencies. This results in some problems in arrangement, such as the separation of the newer methods of treating burns, which appear under General Emergencies, from another discussion of burns which appears under Home and Farm Accidents, the latter dealing principally with prevention—use of matches, hot liquids and the like. This is, however, a minor drawback for any one who reads through the whole book. The section on the control of hemorrhage by pressure over blood vessels is illustrated by an osseous skeleton rather than the conventional figure showing the blood vessels. Many sections are delightfully illustrated with little sketches which resemble cartoons and which carry their message well. The final section includes chapters on administration in army hospitals, organization of the army medical department and similar discussions, which should prove invaluable for any nurse about to enter one of the services. The book can be recommended to nurses whether in civil or military life.

Public Health Statistics. By Marguerite F. Hall, M.A., Ph.D., Assistant Professor of Public Health Statistics, School of Public Health, University of Michigan, Ann Arbor. Cloth. Price, $5.50. Pp. 408, with 41 illustrations. New York & London: Paul B. Hoeber, Inc., 1942.

In the field of public health even more than in that of clinical and laboratory research a thorough knowledge of the handling of statistics is imperative. This book has combined a common sense view on the interpretation of public health statistics with a clear and concise presentation of the algebra involved. Miss Hall, who is assistant professor of public health statistics in the School of Public Health at the University of Michigan, gives prominence to the limitations of the statistical method by citing Quetelet's four rules: 1. Have no preconceived ideas. Be unbiased. Attack your problem with an open mind. 2. Don't reject contrary values. Eliminate possible errors; then seek verification of the contrary values. 3. Face the facts you find. 4. Compare data that are comparable. Accurate comparison can be made only between similar things and over short periods of time. Data drawn from unlike sources may lead to false interpretations. These rules are sound for any scientific method, and the fact that they are applied to statistics is merely evidence of the scientific acceptability of statistical methodology.

Of special interest to prospective contributors to THE JOURNAL is the following exercise given at the end of one of the chapters: "Select a table published in THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION. Give its fundamental weaknesses and make a skeleton table which would more nearly conform to the theoretical ideals of statistical tabulation. . . ." Though not all tables in THE JOURNAL can be used as horrible examples, most writers on clinical subjects have been inclined to neglect the principles of proper statistical treatment of their data. Herein lies a useful reminder.

Bernard, creador de la medicina científica: Estudio crítico de su labor científica, seguido de una versión castellana de su Introducción al estudio de la medicina experimental. Por el Coronel M. C. Jose Joaquin Izquierdo, profesor de fisiología experimental en la Escuela médico militar y en la Facultad de medicina de la Universidad nacional de México, México, D. F. Paper. Price, 20 pesos. Pp. 329. Mexico, D. F.: Imprenta Universitaria de México, 1942.

The interest in Claude Bernard on the part of Mexican investigators is praiseworthy. The first translation of Introduction à l'étude de la médecine expérimentale (Paris, 1865) appeared in Mexico in 1880. The second and more concise translation, itself a classic, by don Carlos Garcia (1900) was published in the somewhat obscure village of San Luis Potosi. The Garcia translation has been missed by most of the collectors of Bernard, and indeed the author of the book under review belatedly admits neglecting the mention of it in his outline of studies in physiology in Mexico, Balance cuatricentenario de la fisiologia en Mexico (1934). The present work is an excellent treatise on Claude Bernard, as it includes not only biographic material but a careful analysis and descriptions of Claude Bernard's most significant experiments. The bibliography, although incomplete, is sufficient to support the text and, on the whole, the book is to be recommended not only to medical historians but to physiologists as well.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

EFFECT ON SKIN OF HEAT AND COLD

To the Editor:—**Please inform me if the tissue changes, such as those due to thermal changes, can be called burns? Specifically, can the changes produced by the action of solidified carbon dioxide on tissue be called a burn? Also what are the essential physiologic and pathologic differences in heat or cold on tissues? I have heard that ice application or hot water bag application makes little difference as used on tissue, as for example in acute appendicitis. In other words, either ice or heat may be used to get the same result.**

M.D., California.

ANSWER.—Changes in the skin from the use of solidified carbon dioxide are often spoken of as burns. Burns as ordinarily understood, however, mean injuries from heat. Pernio is a term often used in connection with the results from exposure to cold. The tissue changes that follow the use of cold differ from those from heat.

According to Sonnenburg and Tschmarke (quoted by Gans, Oskar: Histologie der Hautkrankheiten, Berlin, Julius Springer, 1925, vol. 1, p. 175) it is customary to divide the frostbites into various grades analogous to those for burns, but it is necessary to bear in mind that this classification is based on a purely superficial resemblance of the symptoms devoid of any pathologic justification. Thus one may distinguish between erythematous, bullous and gangrenous dermatitis. The first is marked by a vascular dilatation following a fleeting constriction. A short period of paleness is followed by a bluish red discoloration, swelling and definite itching of the skin, the result of a passive hyperemia. In this condition complete restitution is still possible. If, however, the action of cold and hence the venous accumulation is continued, the increased swelling will be associated with anesthesia of the whole area. Later the formation of serous vesicles is noted, developing into hemorrhagic ones if the damage is deeper. Their disintegration is followed by long lasting ulcers—the second stage of the freezing. At this stage a certain forecast of consequences is no longer possible, since these sequels are largely correlated with impairment of the vessels, which can be gaged only in the course of time. The highest degree of freezing is marked by a deep blue-red discoloration of the whole skin, which is completely anesthetized. A necrosis involving cutis, subcutis and often also the muscles, even all the soft parts together with the bony structure, may lead to the destruction of whole parts. This necrosis usually appears as a dry or moist gangrene, depending on whether the elimination proceeds aseptically or with a secondary infection with all its consequences.

SULFUR PREPARATIONS USED FOR MITES AND HUMAN HEALTH

To the Editor:—**Kindly let me know whether or not there are any health hazards to workers on citrus groves, connected with the spraying or dusting of sulfur preparations for the control of rust mites. The preparations used are a fine sulfur dust, a so-called "wettable sulfur" and a "lime sulfur."**

Edward J. Kempf, M.D., Wading River, L. I., N. Y.

ANSWER.—"Wettable sulfur" is sulfur which has been ground with some wetting agent so that on addition of water the mixture is wet easily and the sulfur does not float on top, as would be the case if plain powdered sulfur was used. The preparation known as "lime sulfur" is a polysulfide of calcium, approximately of the formula CaS_5, made by boiling sulfur with lime and filtering.

The use of wettable sulfur preparations under ordinary field conditions should involve no special health hazard except, possibly, for an occasional instance of sulfur dermatitis in hypersensitive persons.

It is possible that in the practical use of lime sulfur small amounts of sulfur dioxide or hydrogen sulfide might be formed. However, as far as can be ascertained the only health hazard from lime sulfur as normally used may be a dermatitis in susceptible individuals. It might be stressed that, in concentrated solution, lime sulfur may act as a powerful depilatory, and at least one instance has been seen in which such a solution caused burns of the skin. In actual use as an insecticide the preparation is used in such dilute form that its caustic effect is probably not noticeable.

DIFFERENTIATION OF SPLENOMEGALY—ASCOLI TREATMENT OF MALARIA

To the Editor:—**A white man aged 53, who has had an enlarged spleen for the past ten years, has been examined by several competent internists and has had appropriate laboratory work-up. The patient's medical history reveals the fact that in 1912 he lived in Tripoli, at which time he was said to have had fever but diagnosis of the condition was not known. He had been in relatively good health until 1932, when he began to suffer from gastric distress and the spleen was found to be enlarged. Since then the spleen has been becoming larger. At the present time it is enlarged down to the iliac crest and is well beyond the umbilicus to the right. In the last two years the patient has had several attacks of severe pain in the left side of the abdomen. The pain was noticed first at movement, and these attacks have been presumably splenic infarction. The patient has been examined thoroughly; several x-ray examinations of the chest and a gastrointestinal series proved negative. Urinalysis has been essentially negative. Complete blood counts revealed moderate anemia. Leukocytes have been normal in type and number, and on no occasions have any basophils or parasites been found in blood smears. A splenic puncture, done five years ago, did not reveal any abnormality. The physical findings revealed the enlarged spleen mentioned and basal congestion in the left lower lobe. The patient has chronic rhinitis and a postnasal drip. The liver edge can just barely be felt. The blood Wassermann reaction was negative. Gastric washings have not revealed any tubercle bacilli. Gastric analyses have been within normal limits. Blood examinations, including coagulation time, bleeding time, calcium and cholesterol determinations, have been within normal limits. The diagnosis is presumed to be either splenic enlargement due to chronic malaria or, possibly, kala-azar or leishmaniasis. The patient has been treated symptomatically by use of tonics and diet. He refuses an operation. The question arises of further treatment, the advisability of roentgen therapy or of the Ascoli treatment. If the Ascoli treatment is to be given, what are the chances of epinephrine injections to be used causing embolic phenomena due to thrombi of spleen, which must have occurred?**

O. J. Pellitteri, M.D., New York.

ANSWER.—This letter implies a query as to diagnosis when it says that the diagnosis is presumed to be either splenic enlargement due to chronic malaria or possibly kala-azar or leishmaniasis. Kala-azar is the visceral form of leishmaniasis, associated with enlargement of the spleen and liver. As in the case of chronic malaria, examination of material obtained by splenic puncture should serve to exclude malaria and kala-azar if the characteristic evidences of these diseases are absent. Even though there is a slight risk of hemorrhage after splenic puncture, it might be worth while to repeat this examination, since it has not been made for five years. The possibility that the symptoms have been caused by schistosomiasis seems improbable unless the patient lived for a long time in northern Africa in a region where he might have been exposed to repeated reinfection. Perhaps it would be worth while to consider again the possibility of this disease. If the three diseases mentioned are definitely excluded, a diagnosis of Banti's disease would seem to be probable, but histoplasmosis or some other form of fungous disease might be considered among the possibilities.

As to the direct question regarding the Ascoli treatment and its possible relationship to infarction of the spleen, in the first place infarction of the spleen is a common symptom of malaria, regardless of the use of epinephrine injections. The Ascoli treatment has been used by a considerable number of authorities. Froilano de Mello (Experimental Studies on the Treatment of Malarial Splenomegalies by the Method of Ascoli, *South African M. J.* **12**:835 [Nov. 26] 1938) published an excellent critical study of the subject and a general review. Many writers have reported groups of cases numbering from about 20 to 400. For the most part the reports fall into two groups: (1) those which are enthusiastic about the results of the treatment and (2) those which noted little or no benefit from its use. A number of authors stress the fact that transitory circulatory disturbances not infrequently result. These most commonly occur after a number of injections have been given. Giuseppe Pizzilo (Malarial Splenomegaly and Venous Thrombosis Treated with Intravenous Epinephrine, abstr. *Trop. Dis. Bull.* **38**:32 [Jan.] 1941) reported failure to obtain reduction in the size of the spleen in a case which subsequently proved fatal. Toward the end of the course of treatment, after the twentieth injection, there was a copious hematemesis followed by abundant melena. Six months later splenectomy was performed and was followed by death. The author attributed the absence of contraction of the spleen after administration of epinephrine to phlebitic thrombosis, which he assumed to have existed prior to the treatment. Only a single published case found seems to have a direct bearing on the question. (Jorge, A. Lourenço, da Silva; José Ferreira, and Leal, A. Estillac: Congestive Splenomegaly with Hemorrhage, abstr. *Trop. Dis. Bull.* **33**:266 [April] 1936). These authors report a case diagnosed as Banti's disease in which administration of epinephrine brought about considerable reduction in the size of the spleen. Subsequent hematemesis was followed

by still further reduction. In this case it was thought that splenic thrombophlebitis had occurred and had been followed by rupture of veins of the gastrosplenic anastomoses. It does not seem necessary to suppose that use of epinephrine caused the thrombophlebitis or the hemorrhage. The fact that only 2 cases of thrombophlebitis which might conceivably be attributed to the use of epinephrine have been found would make it appear that the risk of such an eventuality is small.

WAR ACTIVITIES OF GIRL SCOUTS AND GIRL GUIDES

To the Editor:—Please send me information as to the duties of the Girl Scouts in civilian emergency; also information as to the English Girl Scouts' activities.

W. J. Tucker, M.D., Ashland, Wis.

ANSWER.—Girl Scouts have taken part in civilian emergency activities in their various localities, meeting the local needs and fitting into the local picture. The composite picture of service given by Girl Scouts throughout the country is as follows: Girl Scouts collected tons of paper and scrap metal in conservation drives, bottles and special materials for clinics, thousands of books for soldiers in camp, old clothes, first aid and invalids' equipment for the Red Cross. They made clothes and quilts for the Red Cross, Needlework Guild and other agencies, cookies and camp kits for soldiers, baby trays and toys for nurseries, bandages and card files for hospitals, surveys of available hospital space and possible emergency bed space, gardens to grow food and herbs needed by welfare groups for medicines and cakes and candy to raise money for relief agencies. They gave welcome to the children of defense workers and refugees, help at home and in day nurseries to release mothers for other jobs, clerical help to social agencies, and gifts and friendship to old folks' homes, orphanages, veterans and other needy families and institutions. No one troop could do all these, but each did some. The older girls from 15 to 18 are organized in groups known as Senior Service Scouts and receive specialized training and give special service in first aid, child care, messenger service, emergency outdoor cooking and, through the Wing Scouts, a newly organized group, make model airplanes and learn how to identify planes.

The Girl Guides of Great Britain have taken an active part in the war effort. These girls have participated in the usual salvage projects in various localities and also were asked by the air ministry to collect empty cotton spools, and collected over two hundred thousand of these. They have helped in harvesting and farming and have also assisted in camouflage projects in small communities and have made use of camouflaging in concealing their own tents in their own small camps. They have helped in teaching "blitz cooking" for family, neighborhood and large canteen groups using improvised fireplaces made from bricks from bombed houses. At the request of the Ministry of Food, demonstrations of this emergency outdoor cooking were given throughout the British Isles.

FLOATING OPACITIES OF EYES

To the Editor:—A white man aged 46, whose previous history is irrelevant, has complained for the past twenty years of seeing small objects floating in front of his eyes, particularly in front of the left eye. He claims that they are small capillaries in which he can distinctly make out red blood corpuscles. Sometimes they are near to his vision and sometimes they seem distant. Together with this he has headaches, mostly over the left frontoparietal region, which are more intense when he is trying to concentrate on his work. His vision is 20/20 in both eyes without glasses. His urine and blood study (Wassermann, blood count and study of blood smear) are negative. Many ophthalmologists have seen him; some called it avitaminosis, while others said it was vitreous bodies floating about the eye chambers. None have, however, been able to give him any relief. He is a sign maker, making both neon and painted signs.

Peter J. Milazzo, M.D., Corona, L. I., N. Y.

ANSWER.—The query does not state whether the floating opacities are actually visible in the vitreous of the patient. If none are visible, the condition is a type of subjective scotoma for which no organic basis has been found. It may be compared to certain tactile sensations without organic cause. It indicates no pathologic condition of the eye and does not really interfere with vision except as an annoyance. Correction of refractive errors, if present, and attention to other possible causes of nervous exhaustion are sometimes of value. The symptom usually becomes much less noticeable and eventually may disappear or be noticed only under exceptional conditions. No relation with avitaminosis is known to exist.

If visible vitreous opacities are present, uveitis must be excluded, but vitreous opacities also occur as part of a presenile degeneration of the vitreous which is common and seldom has any serious consequences.

EGG WHITE IN TREATMENT OF CANCER

To the Editor:—There appeared in the New York *Times* of Dec. 2, 1942 an article entitled "Egg Whites Tested as Cancer Relief." I have a patient with carcinoma of the bladder who has been operated on and irradiated at a large Clinic. His prognosis, as we all know, is hopeless, with a gradual decline day by day. Yesterday his wife came to my office with the article mentioned and asked if there was anything in it that would give her husband any relief or comfort. I advised her that as far as I knew there was nothing to this treatment, but, to ease her mind, will you kindly tell me the merits of the article or of the treatment?

M.D., New York.

ANSWER.—The theoretical basis for the use of egg white in the treatment of cancer depends on five observations:

1. The biotin content of some tumor tissue was found to be greater than that of normal tissue of the same origin.

2. Temporary regressions of new growth have been reported rarely to follow intercurrent infections.

3. Certain infectious agents, particularly bacteria, are known to use biotin in their metabolism.

4. Biotin has been found to have a weak effect in inhibiting the protective effect by certain dietary constituents against liver cancer caused in the rat by the administration of dimethylaminoazobenzene.

5. A protein known as avidin, contained in egg white. may combine with and inactivate biotin.

The feeding of egg white to small animals induces a biotin deficiency. Woglom fed mice with cancer sufficient avidin to eliminate biotin effect in their bodies completely. Even during this period new metastases appeared. There is no reason to suppose from the evidence available that the feeding of egg white or its protein constituent, avidin, to man or animals will cause any change in the course of a neoplastic growth. The single exception to this statement is the report by Kaplan, recently discussed before the Radiological Society of North America. No confirmations of Kaplan's observations have been published.

SHOCK VERSUS INFECTION IN TREATMENT OF COMPOUND FRACTURE

To the Editor:—There is some question in my mind regarding the early treatment of compound fractures. I know the Orr-Trueta technic and feel that I can apply this method when given the proper instruments and hospital. However, it is the early treatment that offers somewhat of a puzzle. Let us assume that our patient is a soldier on the battlefield. His wound is a compound fracture with a protruding bone. The area around the fracture is quite dirty, and perhaps there is a piece of shell and cloth within the wound. An aid man or litter group, equipped with splints, encountered him. Now, should the wound be simply covered with a sterile dressing and the patient gently placed on a litter with some support like a pillow or coat, or should traction and splints be applied regardless of whether the protruding bone might be drawn into the wound? This phase of treatment has troubled me no end. I have felt that it might be wise to place about 10 Gm. of sulfanilamide in the wound, apply traction and splints and send the patient on to a hospital, if possible, where proper treatment can be given. Shall we sacrifice shock prevention by no immobilization and thus tend to prevent infection, or shall we avoid shock and gamble on infection by immobilization? It must be one or the other. I myself should rather place sulfanilamide in the wound, apply splints and avoid shock.

M.D., Massachusetts.

ANSWER.—The conclusion that it is better to avoid shock and gamble on infection by immobilization in fixed traction in a Thomas leg splint, even if bone fragments are drawn back into the wound, is correct and orthodox. Thus treated, not only is shock lessened but pain, possible hemorrhage and avoidable motion at the fracture site leading to churning of the tissues by bone fragments may be eliminated. The sulfanilamide, if obtainable, is highly desirable to spread into the wound, which is covered with a sterile dressing.

BASAL METABOLISM IN NERVOUS PATIENT

To the Editor:—Will the administration of a small amount of sodium bromide or of phenobarbital to an apprehensive patient for sedative purposes shortly before a basal metabolic determination affect the results undesirably? The patient I have in mind has no conclusive signs or symptoms of hyperthyroidism.

M.D., Colorado.

ANSWER.—The administration of a small dose of sodium bromide or of phenobarbital probably will not have much effect on the basal metabolism readings of the patient described. The best way to get a good reading of an apprehensive patient is by frequent determinations of the basal metabolism on different days. In fact, little attention should be paid to a single test of any patient. The important observation is the level of metabolism.